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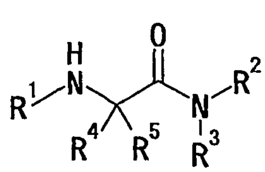
(54) Title: DIPEPTIDYL PEPTIDASE IV INHIBITOR



[I]

(57) Abstract: A compound of the formula [I] wherein each symbol is as defined in the specification, or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof show a DPP-IV inhibitory activity and are novel compounds effective for the treatment of type II diabetes, obesity and the like.

DESCRIPTION

DIPEPTIDYL PEPTIDASE IV INHIBITOR

TECHNICAL FIELD

The present invention relates to a compound useful as a dipeptidyl peptidase IV inhibitor and a dipeptidyl peptidase IV inhibitor.

BACKGROUND ART

Aminopeptidase in a wide sense, which liberates the N-terminal amino acid from proteins and peptides, includes aminopeptidase (hereinafter to be abbreviated as "AP") that liberates one residue, dipeptidyl peptidase (hereinafter to be abbreviated as "DPP") that liberates two residues, and tripeptidyl peptidase (hereinafter to be abbreviated as "TPP") that liberates three residues.

AP is classified into arginyl aminopeptidase, methionyl aminopeptidase, aspartyl aminopeptidase, alanyl aminopeptidase, glutamyl aminopeptidase, prolyl aminopeptidase, leucyl aminopeptidase and cystinyl aminopeptidase based on the substrate specificity. In general, the substrate specificities of these often overlap with each other.

DPP includes four kinds of enzymes of DPP-I, DPP-II, DPP-III and DPP-IV, based on the differences in the substrate specificity thereof, physicochemical properties and intracellular localization. Moreover, the presence of DPP-VI, DPP-VIII, DPP-IX and DPP-X has been recently reported in a literature. TPP includes two kinds of enzymes of TPP-I and TPP-II, based on the differences in the substrate specificity, molecular weight and intracellular localization.

Dipeptidyl peptidase IV (EC3.4.14.5, hereinafter to be abbreviated as "DPP-IV") is a glycoprotein on a cell surface, which has been found as a T cell activated antigen and which is a serine protease that cleaves the second peptide bond on C-terminal from N-terminal of protein and peptide having an X-Pro or X-Ala structure on the N-terminus. DPP-IV is widely distributed in the

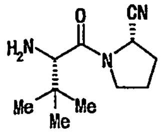
kidney, liver, salivary glands, connective tissues and the like, and is also present in body fluids such as serum, urine, saliva and the like. In the immune system, moreover, it has been clarified that DPP-IV is the same molecule as a T cell activated antigen CD26.

Various physiological roles of DPP-IV have been reported, such as degradation of neuropeptide, activation of T cell, adhesion of metastatic tumor cell to endothelium, penetration of HIV virus into lymphocytes and the like. Notably, the role of inactivating glucagons-like peptide-1 (hereinafter to be abbreviated as "GLP-1") has been attracting attention.

GLP-1 is released from enteroendocrine L-cells in the distal small intestine and colon in response to oral ingestion of nutrients. Active GLP-1 is rapidly converted to inactive GLP-1 by the action of DPP-IV that cleaves the N-terminal dipeptide(His-Ala) of active GLP-1. It is considered that this inactive GLP-1 acts as an antagonist and shows an antagonistic action against GLP-1 receptor, thus suppressing the function of GLP-1 (see, Journal of Clinical Endocrinology and Metabolism, 80(3), 952-957 (1995), American Journal of Physiology, 271, E458-E464 (1996), European Journal of Pharmacology, 318, 429-435 (1996), Diabetes, 47(11), 1663-1670 (1998)).

Suppression of degradation of GLP-1 by inhibiting DPP-IV is considered to be the most preferable method as a means to enhance GLP-1 action. That is, reports have documented that a DPP-IV inhibitor can enhance glucose-dependent insulin secretion and improve glucose tolerance in non-insulin-dependent diabetes mellitus (NIDDM) and in various diabetic animal models, and it can be a superior pharmaceutical agent that improve postprandial hyperglycemia, which is unaccompanied by side effects such as persistent hypoglycemia and the like.

As a DPP-IV inhibitor, the following compounds are known.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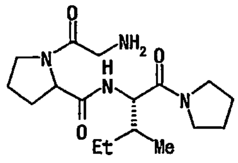
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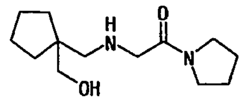
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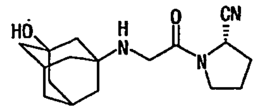
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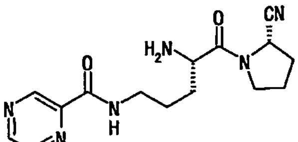
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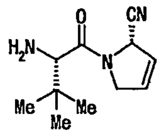
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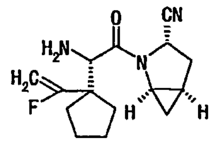
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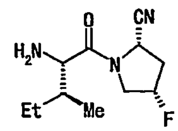
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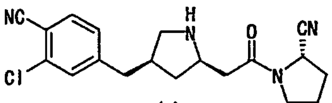
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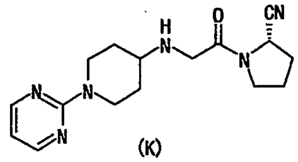
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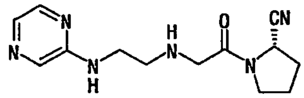
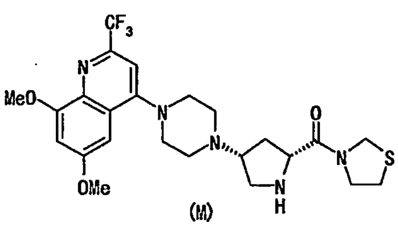

(L)

[compound (A): WO95/15309, JP-A-9-509921, USP5939560, EP731789A, compound (B): WO99/67278, US2002/049164A, EP1087991A, compound (C): USP6124305, compound (D): WO00/34241, JP-A-2002-531547, USP6166063, EP1137635A, compound (E): WO01/81304, EP1282600A, compound (F): WO01/55105, JP-A-2003-520849, US2001/031780A, USP6380398, EP1254113A, compound (G): WO01/68603, US2002/019411A, USP6395767, EP1261586A, compound (H): WO02/38541, compound (J): WO02/14271, EP1308439A, compound (K): WO02/30890, EP1323710A, compound (L): WO02/051836]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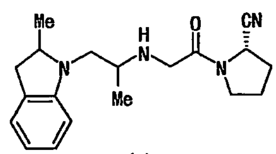
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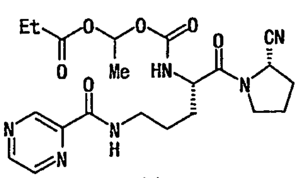
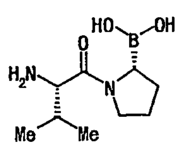
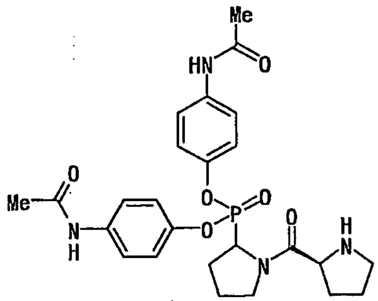

(O)

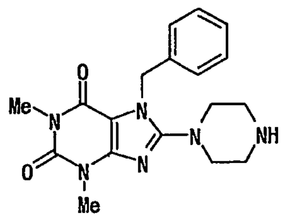

(P)

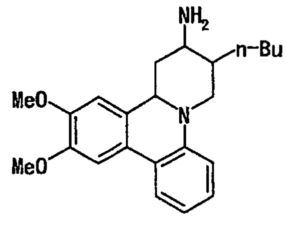
[compound (M): WO03/024942, compound (N): WO03/037327, compound (O): WO03/035067, compound (P): WO03/045228]

All of these have proline or a derivative thereof as a basic structure and is essentially different from the present invention.

Besides these, the following compounds having a completely different structure from the present invention are also known.

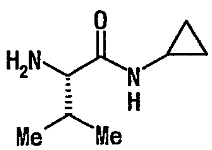

(Q)


(R)


(S)

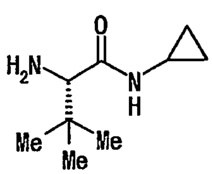
[compound (Q): WO99/46272, JP-A-2002-506075, US2002/061839A, EP1062222A, compound (R): WO02/02560, US2002/161001A, EP1301187A, compound (S): WO03/055881]

On the other hand,

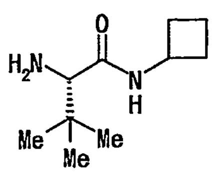

(T)

is described as an intermediate for the production of a protease inhibitor in WO98/45330, JP-A-2002-504094, USP6291687, US2001/044547A, USP6489364 and EP1005493A.

Furthermore,

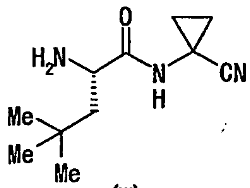

(U)

and


(V)

is described as an intermediate for the production of a matrix metalloproteinase inhibitor in WO96/06074, JP-A-10-504821, USP5763621, EP777646A and EP777646B.

Moreover,



(W)

is described as an intermediate for the production of a cathepsins inhibitor in WO03/029200.

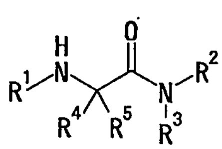
DISCLOSURE OF THE INVENTION

The present invention aims at providing a superior DPP-IV inhibitor. In addition, the present invention aims at providing a compound showing a DPP-IV inhibitory activity and effective for the treatment of diabetes, especially type II diabetes, as well as hyperglycemia, hypoglycemia, Syndrome X, diabetic complications, hyperinsulinemia, obesity, atherosclerosis and related diseases thereof, anxiety, eating disorders, neurodegenerative diseases, as well as various immunomodulatory diseases including psoriasis, multiple sclerosis, rheumatoid arthritis, and chronic inflammatory bowel disease, for organ transplantation, and the like.

The present inventors have conducted intensive studies to solve the above-mentioned problems and found that a compound represented by the following formula [I] (hereinafter sometimes to be referred to as "compound [I]") has a superior DPP-IV inhibitory activity, which resulted in the completion of the present invention. While many of the conventionally known DPP-IV inhibitors have proline as a basic structure, the present invention is a DPP-IV inhibitor having a completely new structure wherein a 5-membered ring of proline is cleaved.

More particularly, the present invention provides the following (1) to (29).

(1) A DPP-IV inhibitor comprising a compound represented by the formula [I]



[I]

wherein

R^1 is selected from the following [A]-[E]:

[A] hydrogen atom,

[B] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <B1>-<B14>),

·<B1> halogen atom,

·<B2> C_{3-12} cycloalkyl,

·<B3> hydroxyl,

·<B4> C_{1-6} alkoxy,

·<B5> C_{1-6} alkylthio,

·<B6> aryloxy,

·<B7> aralkyloxy,

·<B8> heterocyclyloxy,

·<B9> heterocyclyl-C_{1-6} alkoxy,

·<B10> nitro,

·<B11> amino,

·<B12> cyano,

·<B13> carboxyl and

·<B14> $-X^1-R^{11}$ (R^{11} is selected from the following (Ba1) and (Ba2) and X^1 is selected from the following (Bb1)-(Bb23)),

··(Ba1) aryl and

··(Ba2) heterocyclyl (said aryl and heterocyclyl are optionally substituted by 1 to 3 substituents selected from the following <Baa1>-<Baa17>),

···<Baa1> halogen atom,

···<Baa2> C_{1-6} alkyl,

···<Baa3> halo-C_{1-6} alkyl,

···<Baa4> C_{3-12} cycloalkyl,

···<Baa5> aralkyl,

···<Baa6> heterocyclyl-C_{1-6} alkyl,

···<Baa7> hydroxyl,

···<Baa8> C_{1-6} alkoxy,

···<Baa9> C_{1-6} alkylthio,

···<Baa10> aryloxy,

···<Baa11> aralkyloxy,

···<Baa12> heterocyclyloxy,

···<Baa13> heterocyclyl-C_{1-6} alkoxy,

···<Baa14> nitro,

···<Baa15> amino,

···<Baa16> cyano and

···<Baa17> carboxyl;

··(Bb1) single bond,

··(Bb2) -O-,

··(Bb3) -S-,

··(Bb4) -NH-,

··(Bb5) -CO-,

··(Bb6) $-CO_2-$,

··(Bb7) -OCO-,

··(Bb8) $-OCO_2-$,

··(Bb9) -SO-,

··(Bb10) $-SO_2-$,

··(Bb11) $-OSO_2-$,

··(Bb12) $-SO_3-$,

··(Bb13) -CONH-,

··(Bb14) -NHCO-,

··(Bb15) -CSNH-,

··(Bb16) -NHCS-,

··(Bb17) $-NHSO_2-$,

··(Bb18) $-SO_2NH-$,

··(Bb19) $-NHCO_2-$,

··(Bb20) -OCONH-,

··(Bb21) -NHCONH-,

··(Bb22) -NHCSNH- and

··(Bb23) $-NHSO_2NH-$;

[C] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <C1>-<C17>),

·<C1> halogen atom,

·<C2> C_{1-6} alkyl,

·<C3> halo-C_{1-6} alkyl,

·<C4> aralkyl,

·<C5> heterocyclyl-C_{1-6} alkyl,

·<C6> hydroxyl,

·<C7> C_{1-6} alkoxy,

·<C8> C_{1-6} alkylthio,

·<C9> aryloxy,

·<C10> aralkyloxy,

·<C11> heterocyclyloxy,

·<C12> heterocyclyl-C_{1-6} alkoxy,

·<C13> nitro,

·<C14> amino,

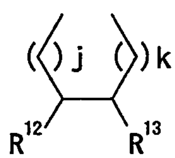
·<C15> cyano,

·<C16> carboxyl and

·<C17> $-X^1-R^{11}$ (R^{11} and X^1 are as defined above);

[D] $-X^1-R^{11}$ (R^{11} and X^1 are as defined above); or

[E]



wherein R^{12} and R^{13} are each independently selected from the following (E1)-(E3), j and k are each independently an integer of 0 to 3, which is formed by R^1 and R^4 in combination,

·(E1) hydrogen atom,

·(E2) $-X^{12}-R^{14}$ (R^{14} is selected from the following (Ea1) and (Ea2), X^{12} is selected from the following (Eb1)-(Eb24)),

··(Ea1) aryl and

··(Ea2) heterocyclyl (said aryl and heterocyclyl are optionally substituted by 1 to 3 substituents selected from the following <Eaa1>-<Eaa17>),

···<Eaa1> halogen atom,

···<Eaa2> C_{1-6} alkyl,

···<Eaa3> halo-C_{1-6} alkyl,

···<Eaa4> C_{3-12} cycloalkyl,

···<Eaa5> aralkyl,

···<Eaa6> heterocyclyl-C_{1-6} alkyl,

···<Eaa7> hydroxyl,

···<Eaa8> C_{1-6} alkoxy,

···<Eaa9> C_{1-6} alkylthio,

···<Eaa10> aryloxy,

···<Eaa11> aralkyloxy,

···<Eaa12> heterocyclyloxy,

···<Eaa13> heterocyclyl-C_{1-6} alkoxy,

···<Eaa14> nitro,

···<Eaa15> amino,

···<Eaa16> cyano and

···<Eaa17> carboxyl;

··(Eb1) single bond,

··(Eb2) –O–,

··(Eb3) –S–,

··(Eb4) –NH–,

··(Eb5) –CO–,

··(Eb6) –CO_2–,

··(Eb7) –OCO–,

··(Eb8) –OCO_2–,

··(Eb9) –SO–,

··(Eb10) –SO_2–,

··(Eb11) –OSO_2–,

··(Eb12) –SO_3–,

··(Eb13) –CONH–,

··(Eb14) –NHCO–,

··(Eb15) –CSNH–,

··(Eb16) –NHCS–,

··(Eb17) –$NHSO_2$–,

··(Eb18) –SO_2NH–,

··(Eb19) –$NHCO_2$–,

··(Eb20) –OCONH–,

••(Eb21) -NHCONH-,

••(Eb22) -NHCSNH-,

••(Eb23) $-NHSO_2NH-$ and

••(Eb24) 4 to 7-membered divalent saturated heterocycle;

or

•(E3) benzene ring formed by R^{12} and R^{13} together with the adjacent carbon atoms (said benzene ring is optionally substituted by 1 to 3 substituents selected from the following <Ec1>-<Ec17>),

••<Ec1> halogen atom,

••<Ec2> C_{1-6} alkyl,

••<Ec3> halo-C_{1-6} alkyl,

••<Ec4> C_{3-12} cycloalkyl,

••<Ec5> aralkyl,

••<Ec6> heterocyclyl-C_{1-6} alkyl,

••<Ec7> hydroxyl,

••<Ec8> C_{1-6} alkoxy,

••<Ec9> C_{1-6} alkylthio,

••<Ec10> aryloxy,

••<Ec11> aralkyloxy,

••<Ec12> heterocyclyloxy,

••<Ec13> heterocyclyl-C_{1-6} alkoxy,

••<Ec14> nitro,

••<Ec15> amino,

••<Ec16> cyano and

••<Ec17> carboxyl;

R^2 is selected from the following [F]-[H]:

[F] hydrogen atom,

[G] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <G1>-<G18>),

•<G1> halogen atom,

•<G2> C_{3-12} cycloalkyl,

•<G3> hydroxyl,

•<G4> C_{1-6} alkoxy,

•<G5> C_{1-6} alkylthio,

- <G6> aryloxy,
- <G7> aralkyloxy,
- <G8> heterocyclyloxy,
- <G9> heterocyclyl-C_{1-6} alkoxy,
- <G10> nitro,
- <G11> amino,
- <G12> cyano,
- <G13> amido,
- <G14> =O,
- <G15> carboxyl,
- <G16> $-PO(OH)_2$,
- <G17> $-PO(O-C_{1-6}$ alkyl$)_2$ and
- <G18> $-PO(O$-aryl$)_2$;

and

[H] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <H1>-<H21>),

- <H1> halogen atom,
- <H2> C_{1-6} alkyl,
- <H3> halo-C_{1-6} alkyl,
- <H4> aralkyl,
- <H5> heterocyclyl-C_{1-6} alkyl,
- <H6> hydroxyl,
- <H7> C_{1-6} alkoxy,
- <H8> C_{1-6} alkylthio,
- <H9> aryloxy,
- <H10> aralkyloxy,
- <H11> heterocyclyloxy,
- <H12> heterocyclyl-C_{1-6} alkoxy,
- <H13> nitro,
- <H14> amino,
- <H15> cyano,
- <H16> amido,
- <H17> =O,
- <H18> carboxyl,

•<H19> $-PO(OH)_2$,

•<H20> $-PO(O-C_{1-6}$ alkyl$)_2$ and

•<H21> $-PO(O-aryl)_2$;

R^3 is selected from the following [I] and [J]

[I] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <I1>-<I18>),

•<I1> halogen atom,

•<I2> C_{3-12} cycloalkyl,

•<I3> hydroxyl,

•<I4> C_{1-6} alkoxy,

•<I5> C_{1-6} alkylthio,

•<I6> aryloxy,

•<I7> aralkyloxy,

•<I8> heterocyclyloxy,

•<I9> heterocyclyl-C_{1-6} alkoxy,

•<I10> nitro,

•<I11> amino,

•<I12> cyano,

•<I13> amido,

•<I14> =O,

•<I15> carboxyl,

•<I16> $-PO(OH)_2$,

•<I17> $-PO(O-C_{1-6}$ alkyl$)_2$ and

•<I18> $-PO(O-aryl)_2$;

and

[J] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <J1>-<J21>),

•<J1> halogen atom,

•<J2> C_{1-6} alkyl,

•<J3> halo-C_{1-6} alkyl,

•<J4> aralkyl,

•<J5> heterocyclyl-C_{1-6} alkyl,

•<J6> hydroxyl,

•<J7> C_{1-6} alkoxy,

·<J8> C_{1-6} alkylthio,

·<J9> aryloxy,

·<J10> aralkyloxy,

·<J11> heterocyclyloxy,

·<J12> heterocyclyl-C_{1-6} alkoxy,

·<J13> nitro,

·<J14> amino,

·<J15> cyano,

·<J16> amido,

·<J17> =O,

·<J18> carboxyl,

·<J19> $-PO(OH)_2$,

·<J20> $-PO(O-C_{1-6}\ alkyl)_2$ and

·<J21> $-PO(O\text{-}aryl)_2$;

R^4 is selected from the following [K]-[S]:

[K] hydrogen atom,

[L] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <L1>-<L14>),

·<L1> halogen atom,

·<L2> C_{3-12} cycloalkyl,

·<L3> hydroxyl,

·<L4> C_{1-6} alkoxy,

·<L5> C_{1-6} alkylthio,

·<L6> aryloxy,

·<L7> aralkyloxy,

·<L8> heterocyclyloxy,

·<L9> heterocyclyl-C_{1-6} alkoxy,

·<L10> nitro,

·<L11> amino,

·<L12> cyano,

·<L13> carboxyl and

·<L14> $-Y^{41}-R^{41}$ (R^{41} is selected from the following (La1)-(La8), and Y^{41} is selected from the following (Lb1) and (Lb2)),

··(La1) hydrogen atom,

··(La2) C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <Laa1>-<Laa24>),

···<Laa1> halogen atom,

···<Laa2> C_{3-12} cycloalkyl,

···<Laa3> hydroxyl,

···<Laa4> aralkyloxy,

···<Laa5> heterocyclyloxy,

···<Laa6> heterocyclyl-C_{1-6} alkoxy,

···<Laa7> nitro,

···<Laa8> cyano,

···<Laa9> carboxyl,

···<Laa10> $-OR^{413}$,

···<Laa11> $-COR^{414}$,

···<Laa12> $-CO_2R^{413}$,

···<Laa13> $-OCOR^{413}$,

···<Laa14> $-CONR^{415}R^{416}$,

···<Laa15> $-OCONR^{415}R^{416}$,

···<Laa16> $-NR^{415}R^{416}$,

···<Laa17> $-NR^{417}COR^{413}$,

···<Laa18> $-NR^{417}CO_2R^{413}$,

···<Laa19> $-SR^{413}$,

···<Laa20> $-SOR^{413}$,

···<Laa21> $-SO_2R^{413}$,

···<Laa22> $-SO_2NR^{415}R^{416}$,

···<Laa23> $-NR^{417}SO_2R^{413}$ and

···<Laa24> $-NR^{417}CONR^{415}R^{416}$

(R^{413} is C_{1-6} alkyl, C_{3-12} cycloalkyl or aryl,

R^{414}, R^{415} and R^{416} are the same or different and each is hydrogen atom, C_{1-6} alkyl, C_{3-12} cycloalkyl or aryl,

R^{417} is hydrogen atom or C_{1-6} alkyl,

or R^{417} in combination with R^{413} form C_{1-4} alkylene);

··(La3) C_{3-12} cycloalkyl;

··(La4) C_{3-12} cycloalkyl-C_{1-6} alkyl;

··(La5) aryl;

··(La6) aralkyl;

··(La7) heterocyclyl and

··(La8) heterocyclyl-C_{1-6} alkyl

(said cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl and heterocyclylalkyl are optionally substituted by 1 to 3 substituents selected from the following <Lab1>-<Lab33>),

···<Lab1> halogen atom,

···<Lab2> C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from hydroxyl, C_{1-6} alkoxy, $-SO_2-C_{1-6}$ alkyl, $-SO_2$-aryl, $-NHSO_2-C_{1-6}$ alkyl and $-NHSO_2$-halo-C_{1-6} alkyl),

···<Lab3> halo-C_{1-6} alkyl,

···<Lab4> aralkyl,

···<Lab5> heterocyclyl-C_{1-6} alkyl,

···<Lab6> C_{3-12} cycloalkyl,

···<Lab7> hydroxyl,

···<Lab8> C_{1-6} alkoxy,

···<Lab9> aralkyloxy,

···<Lab10> heterocyclyloxy,

···<Lab11> heterocyclyl-C_{1-6} alkoxy,

···<Lab12> nitro,

···<Lab13> amino,

···<Lab14> cyano,

···<Lab15> carboxyl,

···<Lab16> (C_{1-6} alkoxy)carbonyl,

···<Lab17> C_{1-6} alkylsulfonyl,

···<Lab18> $-CH_2CO_2H$,

···<Lab19> $-OR^{413}$,

···<Lab20> $-COR^{414}$,

···<Lab21> $-CO_2R^{413}$,

···<Lab22> $-OCOR^{413}$,

···<Lab23> $-CONR^{415}R^{416}$,

···<Lab24> $-OCONR^{415}R^{416}$,

···<Lab25> $-NR^{415}R^{416}$,

···<Lab26> $-NR^{417}COR^{413}$,

···<Lab27> $-NR^{417}CO_2R^{413}$,

···<Lab28> $-SR^{413}$,

···<Lab29> $-SOR^{413}$,

···<Lab30> $-SO_2R^{413}$,

···<Lab31> $-SO_2NR^{415}R^{416}$,

···<Lab32> $-NR^{417}SO_2R^{413}$ and

···<Lab33> $-NR^{417}CONR^{415}R^{416}$

(R^{413}, R^{414}, R^{415}, R^{416} and R^{417} are as defined above);

··(Lb1) single bond and

··(Lb2) X^{41} (X^{41} is $-(CHR^{418})_c-X^{41a}-(CHR^{419})_d-$, X^{41a} is selected from the following (Lba1)-(Lba23), R^{418} and R^{419} are the same or different and each is hydrogen atom or C_{1-6} alkyl, c is an integer of 0 to 2, and d is an integer of 0 to 4),

···(Lba1) -O-,

···(Lba2) -S-,

···(Lba3) -CO-,

···(Lba4) $-CO_2-$,

···(Lba5) -OCO-,

···(Lba6) $-OCO_2-$,

···(Lba7) -SO-,

···(Lba8) $-SO_2-$,

···(Lba9) $-OSO_2-$,

···(Lba10) $-SO_3-$,

···(Lba11) $-NR^{411}-$,

···(Lba12) $-CONR^{411}-$,

···(Lba13) $-NR^{411}CO-$,

···(Lba14) $-CSNR^{411}-$,

···(Lba15) $-NR^{411}CS-$,

···(Lba16) $-SO_2NR^{411}-$,

···(Lba17) $-NR^{411}SO_2-$,

···(Lba18) $-OCONR^{411}-$,

···(Lba19) $-NR^{411}CO_2-$,

···(Lba20) $-NR^{411}CONR^{412}-$,

···(Lba21) $-NR^{411}CSNR^{412}-$,

···(Lba22) $-NR^{411}SO_2NR^{412}-$ (R^{411} and R^{412} are the same or different and each is selected from the following (Lbaa1)-(Lbaa3)),

····(Lbaa1) hydrogen atom,

····(Lbaa2) C_{1-6} alkyl (alkyl is optionally substituted by 1 to 3 substituents selected from the following <Lbaaa1>-<Lbaaa14>),

·····<Lbaaa1> halogen atom,

·····<Lbaaa2> C_{3-12} cycloalkyl,

·····<Lbaaa3> hydroxyl,

·····<Lbaaa4> C_{1-6} alkoxy,

·····<Lbaaa5> C_{1-6} alkylthio,

·····<Lbaaa6> aryloxy,

·····<Lbaaa7> aralkyloxy,

·····<Lbaaa8> heterocyclyloxy,

·····<Lbaaa9> heterocyclyl-C_{1-6} alkoxy,

·····<Lbaaa10> nitro,

·····<Lbaaa11> amino,

·····<Lbaaa12> cyano,

·····<Lbaaa13> carboxyl,

·····<Lbaaa14> oxo; and

····(Lbaa3) $-(CH_2)_p-$ (p is an integer of 1 to 3) formed by R^{411} and R^{412} in combination; and

···(Lba23) 4 to 7-membered divalent saturated heterocycle;

[M] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <M1>-<M18>),

·<M1> halogen atom,

·<M2> C_{1-6} alkyl,

·<M3> halo-C_{1-6} alkyl,

·<M4> aralkyl,

·<M5> heterocyclyl-C_{1-6} alkyl,

·<M6> hydroxyl,

·<M7> C_{1-6} alkoxy,

·<M8> C_{1-6} alkylthio,

·<M9> aryloxy,

·<M10> aralkyloxy,

·<M11> heterocyclyloxy,

·<M12> heterocyclyl-C_{1-6} alkoxy,

·<M13> azido,

·<M14> nitro,

·<M15> amino,

·<M16> cyano,

·<M17> carboxyl and

·<M18> $-Y^{42}-R^{41}$ (R^{41} is as defined above, and Y^{42} is selected from the following (Ma1)-(Ma12)),

··(Ma1) single bond,

··(Ma2) $-X^{41}-$,

··(Ma3) $-Z^{41}-$,

··(Ma4) $-Z^{41}-Z^{42}-$,

··(Ma5) $-X^{41}-Z^{41}-$,

··(Ma6) $-Z^{41}-X^{41}-$,

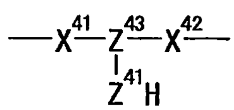
··(Ma7) $-X^{41}-Z^{41}-X^{42}-$,

··(Ma8) $-X^{41}-Z^{41}-Z^{42}-$,

··(Ma9) $-Z^{41}-X^{41}-Z^{42}-$,

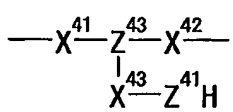
··(Ma10) $-Z^{41}-Z^{42}-X^{41}-$,

··(Ma11)



and

··(Ma12)



(X^{41} is as defined above, X^{42} and X^{43} are each independently $-(CHR^{420})_e-X^{42a}-(CHR^{421})_f-$, X^{42a} is selected from the following (Maa1)-(Maa23), R^{420} and R^{421} are the same or different and each is hydrogen atom or C_{1-6} alkyl, e and f are each independently an integer of 0 to 2, Z^{41} and Z^{42} are the same or different and each is selected from the following (Mab1)-(Mab6), and Z^{43} is selected

from the following (Mac1)-(Mac5)),

···(Maa1) single bond,

···(Maa2) -O-,

···(Maa3) -S-,

···(Maa4) -CO-,

···(Maa5) $-CO_2-$,

···(Maa6) -OCO-,

···(Maa7) $-OCO_2-$,

···(Maa8) -SO-,

···(Maa9) $-SO_2-$,

···(Maa10) $-OSO_2-$,

···(Maa11) $-SO_3-$,

···(Maa12) $-NR^{411}-$,

···(Maa13) $-CONR^{411}-$,

···(Maa14) $-NR^{411}CO-$,

···(Maa15) $-NR^{411}CO_2-$,

···(Maa16) $-OCONR^{411}-$,

···(Maa17) $-CSNR^{411}-$,

···(Maa18) $-NR^{411}CS-$,

···(Maa19) $-SO_2NR^{411}-$,

···(Maa20) $-NR^{411}SO_2-$,

···(Maa21) $-NR^{411}CONR^{412}-$,

···(Maa22) $-NR^{411}CSNR^{412}-$ and

···(Maa23) $-NR^{411}SO_2NR^{412}-$ (R^{411} and R^{412} are as defined above);

···(Mab1) C_{1-6} alkylene,

···(Mab2) C_{2-6} alkenylene,

···(Mab3) C_{2-6} alkynylene (said alkylene, alkenylene and alkynylene are optionally substituted by 1 to 3 substituents selected from the following <Maba1>-<Maba13>),

····<Maba1> halogen atom,

····<Maba2> C_{3-12} cycloalkyl,

····<Maba3> hydroxyl,

····<Maba4> C_{1-6} alkoxy,

····<Maba5> C_{1-6} alkylthio,

····<Maba6> aryloxy,

····<Maba7> aralkyloxy,

····<Maba8> heterocyclyloxy,

····<Maba9> heterocyclyl-C_{1-6} alkoxy,

····<Maba10> nitro,

····<Maba11> amino,

····<Maba12> cyano and

····<Maba13> carboxyl;

···(Mab4) C_{3-12} cycloalkylene,

···(Mab5) arylene and

···(Mab6) divalent heterocycle (said cycloalkylene, arylene and heterocycle are optionally substituted by 1 to 3 substituents selected from the following <Mabb1>-<Mabb18>),

····<Mabb1> halogen atom,

····<Mabb2> C_{1-6} alkyl,

····<Mabb3> halo-C_{1-6} alkyl,

····<Mabb4> aralkyl,

····<Mabb5> heterocyclyl-C_{1-6} alkyl,

····<Mabb6> C_{3-12} cycloalkyl,

····<Mabb7> hydroxyl,

····<Mabb8> C_{1-6} alkoxy,

····<Mabb9> C_{1-6} alkylthio,

····<Mabb10> aryloxy,

····<Mabb11> aralkyloxy,

····<Mabb12> heterocyclyloxy,

····<Mabb13> heterocyclyl-C_{1-6} alkoxy,

····<Mabb14> nitro,

····<Mabb15> amino,

····<Mabb16> cyano,

····<Mabb17> carboxyl and

····<Mabb18> $-X^{4c}-R^{4c}$ (R^{4c} is selected from the following (Mabba1)-(Mabba4), and X^{4c} is selected from the following (Mabbb1)-(Mabbb9)),

·····(Mabba1) hydrogen atom,

·····(Mabba2) C_{1-6} alkyl,

·····(Mabba3) aryl and

·····(Mabba4) aralkyl (alkyl, aryl and aralkyl are optionally substituted by 1 to 3 substituents selected from the following <Mabbaa1>-<Mabbaa4>)

······<Mabbaa1> halogen atom,

······<Mabbaa2> carboxyl,

······<Mabbaa3> (C_{1-6} alkoxy)carbonyl and

······<Mabbaa4> C_{1-6} alkylsulfonyl;

·····(Mabbb1) single bond,

·····(Mabbb2) -CO-,

·····(Mabbb3) $-CO_2-$,

·····(Mabbb4) -OCO-,

·····(Mabbb5) $-CONR^{41c}-$,

·····(Mabbb6) $-NR^{41c}CO-$,

·····(Mabbb7) $-SO_2-$,

·····(Mabbb8) $-SO_2NR^{41c}-$ and

·····(Mabbb9) $-NR^{41c}SO_2-$ (R^{41c} is hydrogen atom or C_{1-6} alkyl);

···(Mac1) C_{1-6} alkanetriyl,

···(Mac2) C_{2-6} alkenetriyl (said alkanetriyl and alkenetriyl are optionally substituted by 1 to 3 substituents selected from the following <Maca1>-<Maca13>)

····<Maca1> halogen atom,

····<Maca2> C_{3-12} cycloalkyl,

····<Maca3> hydroxyl,

····<Maca4> C_{1-6} alkoxy,

····<Maca5> C_{1-6} alkylthio,

····<Maca6> aryloxy,

····<Maca7> aralkyloxy,

····<Maca8> heterocyclyloxy,

····<Maca9> heterocyclyl-C_{1-6} alkoxy,

····<Maca10> nitro,

····<Maca11> amino,

····<Maca12> cyano and

····<Maca13> carboxyl;

···(Mac3) C_{3-12} cycloalkanetriyl,

···(Mac4) arenetriyl and

···(Mac5) trivalent heterocycle (said cycloalkanetriyl, arenetriyl and heterocycle are optionally substituted by 1 to 3 substituents selected from the following <Macb1>-<Macb18>),

····<Macb1> halogen atom,

····<Macb2> C_{1-6} alkyl,

····<Macb3> halo-C_{1-6} alkyl,

····<Macb4> aralkyl,

····<Macb5> heterocyclyl-C_{1-6} alkyl,

····<Macb6> C_{3-12} cycloalkyl,

····<Macb7> hydroxyl,

····<Macb8> C_{1-6} alkoxy,

····<Macb9> C_{1-6} alkylthio,

····<Macb10> aryloxy,

····<Macb11> aralkyloxy,

····<Macb12> heterocyclyloxy,

····<Macb13> heterocyclyl-C_{1-6} alkoxy,

····<Macb14> nitro,

····<Macb15> amino,

····<Macb16> cyano,

····<Macb17> carboxyl and

····<Macb18> $-CH_2CO_2H$;

[N] aryl,

[O] aralkyl,

[P] heterocyclyl,

[Q] heterocyclyl-C_{1-6} alkyl (said aryl, aralkyl, heterocyclyl and heterocyclyl-C_{1-6} alkyl are optionally substituted by 1 to 3 substituents selected from the following <N1>-<N19>),

·<N1> halogen atom,

·<N2> C_{1-6} alkyl,

·<N3> C_{3-12} cycloalkyl,

·<N4> halo-C_{1-6} alkyl,

·<N5> aralkyl,

·<N6> heterocyclyl-C_{1-6} alkyl,

·<N7> hydroxyl,

·<N8> C_{1-6} alkoxy,

·<N9> C_{1-6} alkylthio,

·<N10> aryloxy,

·<N11> aralkyloxy,

·<N12> heterocyclyloxy,

·<N13> heterocyclyl-C_{1-6} alkoxy,

·<N14> nitro,

·<N15> amino,

·<N16> cyano,

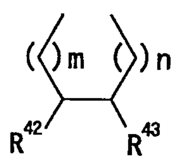
·<N17> =O,

·<N18> carboxyl and

·<N19> $-Y^{42}-R^{41}$ (R^{41} and Y^{42} are as defined above);

[R] $-Y^{41}-R^{41}$ (R^{41} and Y^{41} are as defined above), or

[S]



(R^{42} and R^{43} are each independently selected from the following (S1)-(S3), and m and n are each independently an integer of 0 to 3) formed by R^4 and R^5 in combination,

·(S1) hydrogen atom,

·(S2) $-Y^{41}-R^{44}$ (R^{44} is selected from the following (Sa1) and (Sa2) and Y^{41} are as defined above),

··(Sa1) aryl and

··(Sa2) heterocyclyl (aryl and heterocyclyl are optionally substituted by 1 to 3 substituents selected from the following <Saa1>-<Saa17>),

···<Saa1> halogen atom,

···<Saa2> C_{1-6} alkyl,

···<Saa3> halo-C_{1-6} alkyl,

···<Saa4> aralkyl,

···<Saa5> heterocyclyl-C_{1-6} alkyl,

···<Saa6> C_{3-12} cycloalkyl,

···<Saa7> hydroxyl,

···<Saa8> C_{1-6} alkoxy,

···<Saa9> C_{1-6} alkylthio,

···<Saa10> aryloxy,

···<Saa11> aralkyloxy,

···<Saa12> heterocyclyloxy,

···<Saa13> heterocyclyl-C_{1-6} alkoxy,

···<Saa14> nitro,

···<Saa15> amino,

···<Saa16> cyano and

···<Saa17> carboxyl;

or

·(S3) benzene ring formed by R^{42} and R^{43} together with the adjacent carbon atoms (said benzene ring is optionally substituted by 1 to 3 substituents selected from the following <Sc1>-<Sc17>),

··<Sc1> halogen atom,

··<Sc2> C_{1-6} alkyl,

··<Sc3> halo-C_{1-6} alkyl,

··<Sc4> aralkyl,

··<Sc5> heterocyclyl-C_{1-6} alkyl,

··<Sc6> C_{3-12} cycloalkyl,

··<Sc7> hydroxyl,

··<Sc8> C_{1-6} alkoxy,

··<Sc9> C_{1-6} alkylthio,

··<Sc10> aryloxy,

··<Sc11> aralkyloxy,

··<Sc12> heterocyclyloxy,

··<Sc13> heterocyclyl-C_{1-6} alkoxy,

··<Sc14> nitro,

··<Sc15> amino,

··<Sc16> cyano and

··<Sc17> carboxyl;

R^5 is selected from the following [T]-[BB],

[T] hydrogen atom,

[U] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <U1>-<U14>),

·<U1> halogen atom,

·<U2> C_{3-12} cycloalkyl,

·<U3> hydroxyl,

·<U4> C_{1-6} alkoxy,

·<U5> C_{1-6} alkylthio,

·<U6> aryloxy,

·<U7> aralkyloxy,

·<U8> heterocyclyloxy,

·<U9> heterocyclyl-C_{1-6} alkoxy,

·<U10> nitro,

·<U11> amino,

·<U12> cyano,

·<U13> carboxyl and

·<U14> $-X^{44}-R^{45}$ (R^{45} is selected from the following (Ua1) and (Ua2), and X^{44} is selected from the following (Ub1)-(Ub23)),

··(Ua1) aryl and

··(Ua2) heterocyclyl (said aryl and heterocyclyl are optionally substituted by 1 to 3 substituents selected from the following <Uaa1>-<Uaa17>)

···<Uaa1> halogen atom,

···<Uaa2> C_{1-6} alkyl,

···<Uaa3> halo-C_{1-6} alkyl,

···<Uaa4> C_{3-12} cycloalkyl,

···<Uaa5> aralkyl,

···<Uaa6> heterocyclyl-C_{1-6} alkyl,

···<Uaa7> hydroxyl,

···<Uaa8> C_{1-6} alkoxy,

···<Uaa9> C_{1-6} alkylthio,

···<Uaa10> aryloxy,

···<Uaa11> aralkyloxy,

···<Uaa12> heterocyclyloxy,

···<Uaa13> heterocyclyl-C_{1-6} alkoxy,

···<Uaa14> nitro,

···<Uaa15> amino,

···<Uaa16> cyano and

···<Uaa17> carboxyl;

··(Ub1) single bond,

··(Ub2) -O-,

··(Ub3) -S-,

··(Ub4) -NH-,

··(Ub5) -CO-,

··(Ub6) $-CO_2-$,

··(Ub7) -OCO-,

··(Ub8) $-OCO_2-$,

··(Ub9) -SO-,

··(Ub10) $-SO_2-$,

··(Ub11) $-OSO_2-$,

··(Ub12) $-SO_3-$,

··(Ub13) -CONH-,

··(Ub14) -NHCO-,

··(Ub15) -CSNH-,

··(Ub16) -NHCS-,

··(Ub17) $-NHSO_2-$,

··(Ub18) $-SO_2NH-$,

··(Ub19) $-NHCO_2-$,

··(Ub20) -OCONH-,

··(Ub21) -NHCONH-,

··(Ub22) -NHCSNH- and

··(Ub23) $-NHSO_2NH-$;

[V] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <V1>-<V17>),

·<V1> halogen atom,

·<V2> C_{1-6} alkyl,

·<V3> halo-C_{1-6} alkyl,

•<V4> aralkyl,

•<V5> heterocyclyl-C_{1-6} alkyl,

•<V6> hydroxyl,

•<V7> C_{1-6} alkoxy,

•<V8> C_{1-6} alkylthio,

•<V9> aryloxy,

•<V10> aralkyloxy,

•<V11> heterocyclyloxy,

•<V12> heterocyclyl-C_{1-6} alkoxy,

•<V13> nitro,

•<V14> amino,

•<V15> cyano,

•<V16> carboxyl and

•<V17> $-X^{44}-R^{45}$ (R^{45} and X^{44} are as defined above);

[W] 3 to 7-membered saturated heterocycle,

[X] aryl,

[Y] heterocyclyl,

[Z] aralkyl,

[AA] heterocyclyl-C_{1-6} alkyl (said saturated heterocycle, aryl, heterocyclyl, aralkyl and heterocyclyl-C_{1-6} alkyl are optionally substituted by 1 to 3 substituents selected from the following <W1>-<W16>),

•<W1> halogen atom,

•<W2> C_{1-6} alkyl,

•<W3> C_{3-12} cycloalkyl,

•<W4> aralkyl,

•<W5> heterocyclyl-C_{1-6} alkyl,

•<W6> hydroxyl,

•<W7> C_{1-6} alkoxy,

•<W8> C_{1-6} alkylthio,

•<W9> aryloxy,

•<W10> aralkyloxy,

•<W11> heterocyclyloxy,

•<W12> heterocyclyl-C_{1-6} alkoxy,

•<W13> nitro,

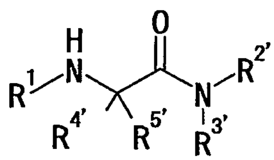
•<W14> amino,

•<W15> cyano and

•<W16> carboxyl; and

[BB] $-X^{44}-R^{45}$ (R^{45} and X^{44} are as defined above), or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

(2) A compound represented by the formula [II]



[II]

wherein R^1 is selected from the following [A]-[E]:

[A] hydrogen atom,

[B] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <B1>-<B14>),

•<B1> halogen atom,

•<B2> C_{3-12} cycloalkyl,

•<B3> hydroxyl,

•<B4> C_{1-6} alkoxy,

•<B5> C_{1-6} alkylthio,

•<B6> aryloxy,

•<B7> aralkyloxy,

•<B8> heterocyclyloxy,

•<B9> heterocyclyl-C_{1-6} alkoxy,

•<B10> nitro,

•<B11> amino,

•<B12> cyano,

•<B13> carboxyl and

•<B14> $-X^1-R^{11}$ (R^{11} and X^1 are defined in the above-mentioned (1));

[C] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <C1>-<C17>),

•<C1> halogen atom,

•<C2> C_{1-6} alkyl,

•<C3> halo-C_{1-6} alkyl,

•<C4> aralkyl,

•<C5> heterocyclyl-C_{1-6} alkyl,

•<C6> hydroxyl,

•<C7> C_{1-6} alkoxy,

•<C8> C_{1-6} alkylthio,

•<C9> aryloxy,

•<C10> aralkyloxy,

•<C11> heterocyclyloxy,

•<C12> heterocyclyl-C_{1-6} alkoxy,

•<C13> nitro,

•<C14> amino,

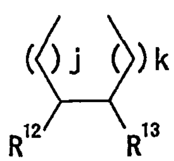
•<C15> cyano,

•<C16> carboxyl and

•<C17> $-X^1-R^{11}$ (R^{11} and X^1 are as defined in the above-mentioned (1));

[D] $-X^1-R^{11}$ (R^{11} and X^1 are as defined in the above-mentioned (1)); or

[E]



wherein R^{12}, R^{13}, j and k are as defined in the above-mentioned (1), which is formed by R^1 and $R^{4'}$ in combination;

$R^{2'}$ is selected from the following [F]-[H],

[F] hydrogen atom,

[G] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <G1>-<G18>),

•<G1> halogen atom,

•<G2> C_{3-12} cycloalkyl,

•<G3> hydroxyl,

•<G4> C_{1-6} alkoxy,

•<G5> C_{1-6} alkylthio,

•<G6> aryloxy,

•<G7> aralkyloxy,

•<G8> heterocyclyloxy,

•<G9> heterocyclyl-C_{1-6} alkoxy,

•<G10> nitro,

•<G11> amino,

•<G12> cyano,

•<G13> amido,

•<G14> =O,

•<G15> carboxyl,

•<G16> $-PO(OH)_2$,

•<G17> $-PO(O-C_{1-6}$ alkyl$)_2$ and

•<G18> $-PO(O$-aryl$)_2$;

[H] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <H1>-<H16> and <H18>-<H21>),

•<H1> halogen atom,

•<H2> C_{1-6} alkyl,

•<H3> halo-C_{1-6} alkyl,

•<H4> aralkyl,

•<H5> heterocyclyl-C_{1-6} alkyl,

•<H6> hydroxyl,

•<H7> C_{1-6} alkoxy,

•<H8> C_{1-6} alkylthio,

•<H9> aryloxy,

•<H10> aralkyloxy,

•<H11> heterocyclyloxy,

•<H12> heterocyclyl-C_{1-6} alkoxy,

•<H13> nitro,

•<H14> amino,

•<H15> cyano,

•<H16> amido,

•<H18> carboxyl,

•<H19> $-PO(OH)_2$,

•<H20> $-PO(O-C_{1-6}$ alkyl$)_2$ and

•<H21> $-PO(O$-aryl$)_2$;

$R^{3'}$ is the following [J]

[J] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <J1>-<J16> and <J18>-<J21>),

•<J1> halogen atom,

•<J2> C_{1-6} alkyl,

•<J3> halo-C_{1-6} alkyl,

•<J4> aralkyl,

•<J5> heterocyclyl-C_{1-6} alkyl,

•<J6> hydroxyl,

•<J7> C_{1-6} alkoxy,

•<J8> C_{1-6} alkylthio,

•<J9> aryloxy,

•<J10> aralkyloxy,

•<J11> heterocyclyloxy,

•<J12> heterocyclyl-C_{1-6} alkoxy,

•<J13> nitro,

•<J14> amino,

•<J15> cyano,

•<J16> amido,

•<J18> carboxyl,

•<J19> $-PO(OH)_2$,

•<J20> $-PO(O-C_{1-6}$ alkyl$)_2$ and

•<J21> $-PO(O$-aryl$)_2$;

$R^{4'}$ is selected from the following [K]-[M], [P], [R] and [S],

[K] hydrogen atom,

[L] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <L1>-<L14>)

•<L1> halogen atom,

•<L2> C_{3-12} cycloalkyl,

•<L3> hydroxyl,

•<L4> C_{1-6} alkoxy,

•<L5> C_{1-6} alkylthio,

•<L6> aryloxy,

•<L7> aralkyloxy,

•<L8> heterocyclyloxy,

•<L9> heterocyclyl-C_{1-6} alkoxy,

•<L10> nitro,

•<L11> amino,

•<L12> cyano,

•<L13> carboxyl and

•<L14> $-Y^{41}-R^{41'}$ ($R^{41'}$ is selected from the following (La1), (La2), (La5) and (La7), and Y^{41} is as defined in the above-mentioned (1)),

••(La1) hydrogen atom,

••(La2) C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <Laa1>-<Laa24>),

•••<Laa1> halogen atom,

•••<Laa2> C_{3-12} cycloalkyl,

•••<Laa3> hydroxyl,

•••<Laa4> aralkyloxy,

•••<Laa5> heterocyclyloxy,

•••<Laa6> heterocyclyl-C_{1-6} alkoxy,

•••<Laa7> nitro,

•••<Laa8> cyano,

•••<Laa9> carboxyl,

•••<Laa10> $-OR^{413}$,

•••<Laa11> $-COR^{414}$,

•••<Laa12> $-CO_2R^{413}$,

•••<Laa13> $-OCOR^{413}$,

•••<Laa14> $-CONR^{415}R^{416}$,

•••<Laa15> $-OCONR^{415}R^{416}$,

•••<Laa16> $-NR^{415}R^{416}$,

•••<Laa17> $-NR^{417}COR^{413}$,

•••<Laa18> $-NR^{417}CO_2R^{413}$,

•••<Laa19> $-SR^{413}$,

•••<Laa20> $-SOR^{413}$,

···<Laa21> $-SO_2R^{413}$,

···<Laa22> $-SO_2NR^{415}R^{416}$,

···<Laa23> $-NR^{417}SO_2R^{413}$ and

···<Laa24> $-NR^{417}CONR^{415}R^{416}$

(R^{413}, R^{414}, R^{415}, R^{416} and R^{417} is as defined in the above-mentioned (1));

··(La5) aryl and

··(La7) heterocyclyl (said aryl and heterocyclyl are optionally substituted by 1 to 3 substituents selected from the following <Lab1>-<Lab33>),

···<Lab1> halogen atom,

···<Lab2> C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from hydroxyl, C_{1-6} alkoxy, $-SO_2-C_{1-6}$ alkyl, $-SO_2$-aryl, $-NHSO_2-C_{1-6}$ alkyl and $-NHSO_2$-halo-C_{1-6} alkyl),

···<Lab3> halo-C_{1-6} alkyl,

···<Lab4> aralkyl,

···<Lab5> heterocyclyl-C_{1-6} alkyl,

···<Lab6> C_{3-12} cycloalkyl,

···<Lab7> hydroxyl,

···<Lab8> C_{1-6} alkoxy,

···<Lab9> aralkyloxy,

···<Lab10> heterocyclyloxy,

···<Lab11> heterocyclyl-C_{1-6} alkoxy,

···<Lab12> nitro,

···<Lab13> amino,

···<Lab14> cyano,

···<Lab15> carboxyl,

···<Lab16> (C_{1-6} alkoxy)carbonyl,

···<Lab17> C_{1-6} alkylsulfonyl,

···<Lab18> $-CH_2CO_2H$,

···<Lab19> $-OR^{413}$,

···<Lab20> $-COR^{414}$,

···<Lab21> $-CO_2R^{413}$,

···<Lab22> $-OCOR^{413}$,

···<Lab23> $-CONR^{415}R^{416}$,

···<Lab24> $-OCONR^{415}R^{416}$,

···<Lab25> $-NR^{415}R^{416}$,

···<Lab26> $-NR^{417}COR^{413}$,

···<Lab27> $-NR^{417}CO_2R^{413}$,

···<Lab28> $-SR^{413}$,

···<Lab29> $-SOR^{413}$,

···<Lab30> $-SO_2R^{413}$,

···<Lab31> $-SO_2NR^{415}R^{416}$,

···<Lab32> $-NR^{417}SO_2R^{413}$ and

···<Lab33> $-NR^{417}CONR^{415}R^{416}$

(R^{413}, R^{414}, R^{415}, R^{416} and R^{417} are as defined in the above-mentioned (1));

[M] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <M1>-<M18>),

·<M1> halogen atom,

·<M2> C_{1-6} alkyl,

·<M3> halo-C_{1-6} alkyl,

·<M4> aralkyl,

·<M5> heterocyclyl-C_{1-6} alkyl,

·<M6> hydroxyl,

·<M7> C_{1-6} alkoxy,

·<M8> C_{1-6} alkylthio,

·<M9> aryloxy,

·<M10> aralkyloxy,

·<M11> heterocyclyloxy,

·<M12> heterocyclyl-C_{1-6} alkoxy,

·<M13> azido,

·<M14> nitro,

·<M15> amino,

·<M16> cyano,

·<M17> carboxyl and

·<M18> $-Y^{42}-R^{41'}$ ($R^{41'}$ is as defined above and Y^{42} is as defined in the the above-mentioned (1));

[P] 3 to 7-membered saturated heterocycle (said saturated heterocycle is optionally substituted by 1 to 3 substituents selected from the following <N1>-<N16> and <N18>),

•<N1> halogen atom,

•<N2> C_{1-6} alkyl,

•<N3> C_{3-12} cycloalkyl,

•<N4> halo-C_{1-6} alkyl,

•<N5> aralkyl,

•<N6> heterocyclyl-C_{1-6} alkyl,

•<N7> hydroxyl,

•<N8> C_{1-6} alkoxy,

•<N9> C_{1-6} alkylthio,

•<N10> aryloxy,

•<N11> aralkyloxy,

•<N12> heterocyclyloxy,

•<N13> heterocyclyl-C_{1-6} alkoxy,

•<N14> nitro,

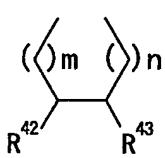
•<N15> amino,

•<N16> cyano and

•<N18> carboxyl;

[R] $-Y^{41}-R^{41'}$ ($R^{41'}$ and Y^{41} are as defined above), or

[S]



(R^{42} and R^{43} are each as defined in the above-mentioned (1), m and n are each independently an integer of 0 to 3) formed by $R^{4'}$ and $R^{5'}$ in combination,

$R^{5'}$ is selected from the following [T]-[W] and [BB],

[T] hydrogen atom,

[U] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <U1>-<U14>),

•<U1> halogen atom,

•<U2> C_{3-12} cycloalkyl,

•<U3> hydroxyl,

•<U4> C_{1-6} alkoxy,

•<U5> C_{1-6} alkylthio,

•<U6> aryloxy,

•<U7> aralkyloxy,

•<U8> heterocyclyloxy,

•<U9> heterocyclyl-C_{1-6} alkoxy,

•<U10> nitro,

•<U11> amino,

•<U12> cyano,

•<U13> carboxyl and

•<U14> $-X^{44}-R^{45}$ (R^{45} and X^{44} are as defined in the above-mentioned (1));

[V] C_{3-12} cycloalkyl (cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <V1>-<V17>),

•<V1> halogen atom,

•<V2> C_{1-6} alkyl,

•<V3> halo-C_{1-6} alkyl,

•<V4> aralkyl,

•<V5> heterocyclyl-C_{1-6} alkyl,

•<V6> hydroxyl,

•<V7> C_{1-6} alkoxy,

•<V8> C_{1-6} alkylthio,

•<V9> aryloxy,

•<V10> aralkyloxy,

•<V11> heterocyclyloxy,

•<V12> heterocyclyl-C_{1-6} alkoxy,

•<V13> nitro,

•<V14> amino,

•<V15> cyano,

•<V16> carboxyl and

•<V17> $-X^{44}-R^{45}$ (R^{45} and X^{44} are as defined in the above-mentioned (1));

[W] 3 to 7-membered saturated heterocycle (said saturated heterocycle is optionally substituted by 1 to 3 substituents selected from the following <W1>-<W16>),

•<W1> halogen atom,

•<W2> C_{1-6} alkyl,

•<W3> C_{3-12} cycloalkyl,

•<W4> aralkyl,

•<W5> heterocyclyl-C_{1-6} alkyl,

•<W6> hydroxyl,

•<W7> C_{1-6} alkoxy,

•<W8> C_{1-6} alkylthio,

•<W9> aryloxy,

•<W10> aralkyloxy,

•<W11> heterocyclyloxy,

•<W12> heterocyclyl-C_{1-6} alkoxy,

•<W13> nitro,

•<W14> amino,

•<W15> cyano and

•<W16> carboxyl;

[BB] $-X^{44}-R^{45}$ (R^{45} and X^{44} are as defined in the above-mentioned (1)), provided that, when R^{1} and $R^{2'}$ are hydrogen atoms and $R^{3'}$ is cyclopropyl, then the combination of one of $R^{4'}$ and $R^{5'}$ being isopropyl or tert-butyl, and the other being hydrogen atom does not occur, and when R^{1} and $R^{2'}$ are hydrogen atoms and $R^{3'}$ is cyclobutyl, then the combination of one of $R^{4'}$ and $R^{5'}$ being tert-butyl, and the other being hydrogen atom does not occur,

or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

(3) The compound of the above-mentioned (2), wherein $R^{41'}$ is selected from the following (La1), (La2), (La5) and (La7), X^{41a} is selected from the following (Lba1)-(Lba23), and other symbols are as defined in the above-mentioned (2),

••(La1) hydrogen atom,

••(La2) C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3

substituents selected from the following <Laa1>-<Laa24>),

···<Laa1> halogen atom,

···<Laa2> C_{3-12} cycloalkyl,

···<Laa3> hydroxyl,

···<Laa4> aralkyloxy,

···<Laa5> heterocyclyloxy,

···<Laa6> heterocyclyl-C_{1-6} alkoxy,

···<Laa7> nitro,

···<Laa8> cyano,

···<Laa9> carboxyl,

···<Laa10> $-OR^{413}$,

···<Laa11> $-COR^{414}$,

···<Laa12> $-CO_2R^{413}$,

···<Laa13> $-OCOR^{413}$,

···<Laa14> $-CONR^{415}R^{416}$,

···<Laa15> $-OCONR^{415}R^{416}$,

···<Laa16> $-NR^{415}R^{416}$,

···<Laa17> $-NR^{417}COR^{413}$,

···<Laa18> $-NR^{417}CO_2R^{413}$,

···<Laa19> $-SR^{413}$,

···<Laa20> $-SOR^{413}$,

···<Laa21> $-SO_2R^{413}$,

···<Laa22> $-SO_2NR^{415}R^{416}$,

···<Laa23> $-NR^{417}SO_2R^{413}$ and

···<Laa24> $-NR^{417}CONR^{415}R^{416}$

(R^{413} is C_{1-6} alkyl, C_{3-12} cycloalkyl or aryl,

R^{414}, R^{415} and R^{416} are the same or different and each is hydrogen atom, C_{1-6} alkyl, C_{3-12} cycloalkyl or aryl,

R^{417} is hydrogen atom or C_{1-6} alkyl);

··(La5) aryl and

··(La7) heterocyclyl (said aryl and heterocyclyl are optionally substituted by 1 to 3 substituents selected from the following <Lab1>-<Lab33>),

···<Lab1> halogen atom,

···<Lab2> C_{1-6} alkyl,

···<Lab3> halo-C_{1-6} alkyl,

···<Lab4> aralkyl,

···<Lab5> heterocyclyl-C_{1-6} alkyl,

···<Lab6> C_{3-12} cycloalkyl,

···<Lab7> hydroxyl,

···<Lab8> C_{1-6} alkoxy,

···<Lab9> aralkyloxy,

···<Lab10> heterocyclyloxy,

···<Lab11> heterocyclyl-C_{1-6} alkoxy,

···<Lab12> nitro,

···<Lab13> amino,

···<Lab14> cyano,

···<Lab15> carboxyl,

···<Lab16> (C_{1-6} alkoxy)carbonyl,

···<Lab17> C_{1-6} alkylsulfonyl,

···<Lab18> $-CH_2CO_2H$,

···<Lab19> $-OR^{413}$,

···<Lab20> $-COR^{414}$,

···<Lab21> $-CO_2R^{413}$,

···<Lab22> $-OCOR^{413}$,

···<Lab23> $-CONR^{415}R^{416}$,

···<Lab24> $-OCONR^{415}R^{416}$,

···<Lab25> $-NR^{415}R^{416}$,

···<Lab26> $-NR^{417}COR^{413}$,

···<Lab27> $-NR^{417}CO_2R^{413}$,

···<Lab28> $-SR^{413}$,

···<Lab29> $-SOR^{413}$,

···<Lab30> $-SO_2R^{413}$,

···<Lab31> $-SO_2NR^{415}R^{416}$,

···<Lab32> $-NR^{417}SO_2R^{413}$ and

···<Lab33> $-NR^{417}CONR^{415}R^{416}$

(R^{413}, R^{414}, R^{415}, R^{416} and R^{417} are as defined above);

···(Lba1) -O-,

···(Lba2) -S-,

···(Lba3) -CO-,

···(Lba4) $-CO_2-$,

···(Lba5) -OCO-,

···(Lba6) $-OCO_2-$,

···(Lba7) -SO-,

···(Lba8) $-SO_2-$,

···(Lba9) $-OSO_2-$,

···(Lba10) $-SO_3-$,

···(Lba11) $-NR^{411}-$,

···(Lba12) $-CONR^{411}-$,

···(Lba13) $-NR^{411}CO-$,

···(Lba14) $-CSNR^{411}-$,

···(Lba15) $-NR^{411}CS-$,

···(Lba16) $-SO_2NR^{411}-$,

···(Lba17) $-NR^{411}SO_2-$,

···(Lba18) $-OCONR^{411}-$,

···(Lba19) $-NR^{411}CO_2-$,

···(Lba20) $-NR^{411}CONR^{412}-$,

···(Lba21) $-NR^{411}CSNR^{412}-$,

···(Lba22) $-NR^{411}SO_2NR^{412}-$ (R^{411} and R^{412} are the same or different and each is selected from the following (Lbaa1)-(Lbaa3)),

····(Lbaa1) hydrogen atom,

····(Lbaa2) C_{1-6} alkyl (alkyl is optionally substituted by 1 to 3 substituents selected from the following <Lbaaa1>-<Lbaaa13>),

·····<Lbaaa1> halogen atom,

·····<Lbaaa2> C_{3-12} cycloalkyl,

·····<Lbaaa3> hydroxyl,

·····<Lbaaa4> C_{1-6} alkoxy,

·····<Lbaaa5> C_{1-6} alkylthio,

·····<Lbaaa6> aryloxy,

·····<Lbaaa7> aralkyloxy,

·····<Lbaaa8> heterocyclyloxy,

·····<Lbaaa9> heterocyclyl-C_{1-6} alkoxy,

·····<Lbaaa10> nitro,

·····<Lbaaa11> amino,

·····<Lbaaa12> cyano,

·····<Lbaaa13> carboxyl, and

····(Lbaa3) $-(CH_2)_p-$ (p is an integer of 1 to 3) formed by R^{411} and R^{412} in combination; and

···(Lba23) 4 to 7-membered divalent saturated heterocycle,

or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

(4) The compound of the above-mentioned (2), wherein R^1 is

[A] hydrogen atom,

[B] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <B1>-<B4>, <B10>-<B12> and <B14>),

·<B1> halogen atom,

·<B2> C_{3-12} cycloalkyl,

·<B3> hydroxyl,

·<B4> C_{1-6} alkoxy,

·<B10> nitro,

·<B11> amino,

·<B12> cyano and

·<B14> $-X^1-R^{11}$ (R^{11} and X^1 are each as defined in the above-mentioned (1)); or

[C] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <C1>, <C2>, <C6>, <C7> and <C13>-<C17>),

·<C1> halogen atom,

·<C2> C_{1-6} alkyl,

·<C6> hydroxyl,

·<C7> C_{1-6} alkoxy,

·<C13> nitro,

·<C14> amino,

·<C15> cyano,

·<C16> carboxyl and

·<C17> $-X^1-R^{11}$ (R^{11} and X^1 are as defined above);

$R^{2'}$ is

[F] hydrogen atom,

[G] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from <G1>-<G4>, <G10>-<G13> and <G16>-<G18>),

·<G1> halogen atom,

·<G2> C_{3-12} cycloalkyl,

·<G3> hydroxyl,

·<G4> C_{1-6} alkoxy,

·<G10> nitro,

·<G11> amino,

·<G12> cyano,

·<G13> amido,

·<G16> $-PO(OH)_2$,

·<G17> $-PO(O-C_{1-6}$ alkyl$)_2$ and

·<G18> $-PO(O$-aryl$)_2$; or

[H] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <H1>, <H2>, <H6>, <H7>, <H13>-<H16> and <H19>-<H21>),

·<H1> halogen atom,

·<H2> C_{1-6} alkyl,

·<H6> hydroxyl,

·<H7> C_{1-6} alkoxy,

·<H13> nitro,

·<H14> amino,

·<H15> cyano,

·<H16> amido,

·<H19> $-PO(OH)_2$,

·<H20> $-PO(O-C_{1-6}$ alkyl$)_2$ and

·<H21> $-PO(O$-aryl$)_2$;

$R^{3'}$ is

[J] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <J1>, <J2>, <J6>, <J7>, <J13>-<J16> and <J19>-<J21>),

•<J1> halogen atom,

•<J2> C_{1-6} alkyl,

•<J6> hydroxyl,

•<J7> C_{1-6} alkoxy,

•<J13> nitro,

•<J14> amino and

•<J15> cyano

•<J16> amido,

•<J19> $-PO(OH)_2$,

•<J20> $-PO(O-C_{1-6}$ alkyl$)_2$ and

•<J21> $-PO(O-aryl)_2$;

$R^{4'}$ is

[K] hydrogen atom,

[L] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <L1>-<L4> and <L10>-<L12>),

•<L1> halogen atom,

•<L2> C_{3-12} cycloalkyl,

•<L3> hydroxyl,

•<L4> C_{1-6} alkoxy,

•<L10> nitro,

•<L11> amino and

•<L12> cyano;

[M] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <M1>, <M2>, <M6>, <M7>, <M13>-<M16> and <M18>),

•<M1> halogen atom,

•<M2> C_{1-6} alkyl,

•<M6> hydroxyl,

•<M7> C_{1-6} alkoxy,

•<M13> azido,

•<M14> nitro,

•<M15> amino,

•<M16> cyano and

・<M18> $-Y^{42}-R^{41'}$ ($R^{41'}$ is as defined in the above-mentioned (2), Y^{42} is as defined in the above-mentioned (1));

[P] 3 to 7-membered saturated heterocycle (said saturated heterocycle is optionally substituted by 1 to 3 substituents selected from the following <N1>, <N2>, <N7>, <N8>, <N14>-<N16> and <N18>),

・<N1> halogen atom,

・<N2> C_{1-6} alkyl,

・<N7> hydroxyl,

・<N8> C_{1-6} alkoxy,

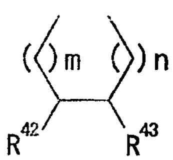
・<N14> nitro,

・<N15> amino,

・<N16> cyano and

・<N18> carboxyl; or

[S]



(R^{42} and R^{43} are each as defined in the above-mentioned (1) and m and n are each independently an integer of 0 to 3) formed by $R^{4'}$ and $R^{5'}$ in combination; and

$R^{5'}$ is

[T] hydrogen atom,

[U] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <U1>-<U4> and <U10>-<U12>),

・<U1> halogen atom,

・<U2> C_{3-12} cycloalkyl,

・<U3> hydroxyl,

・<U4> C_{1-6} alkoxy,

・<U10> nitro,

・<U11> amino and

・<U12> cyano; or

[V] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <V1>, <V2>, <V6>, <V7> and <V13>-<V15>),

·<V1> halogen atom,

·<V2> C_{1-6} alkyl,

·<V6> hydroxyl,

·<V7> C_{1-6} alkoxy,

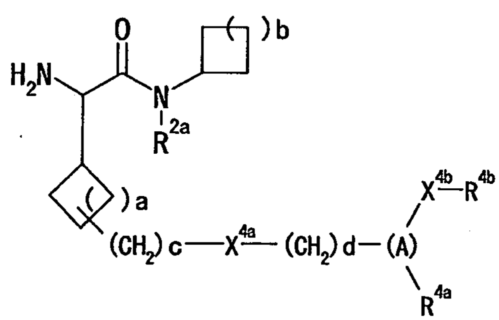
·<V13> nitro,

·<V14> amino and

·<V15> cyano

provided that, when R^1 and $R^{2'}$ are hydrogen atoms and $R^{3'}$ is cyclopropyl, then the combination of one of $R^{4'}$ and $R^{5'}$ being isopropyl or tert-butyl, and the other being hydrogen atom does not occur, and when R^1 and $R^{2'}$ are hydrogen atoms and $R^{3'}$ is cyclobutyl, then the combination of one of $R^{4'}$ and $R^{5'}$ being tert-butyl, and the other being hydrogen atom does not occur, or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

(5) A compound represented by the formula [III]



[III]

wherein R^{2a} is

[F] hydrogen atom or

[G] C_{1-6} alkyl,

R^{4a} is selected from the following [Mabb0], [Mabb1] and [Mabb18],

[Mabb0] hydrogen atom,

[Mabb1] halogen atom and

[Mabb18] $-X^{4c}-R^{4c}$ (R^{4c} is selected from the following (Mabba1)-(Mabba4), X^{4c} is selected from the following (Mabbb1)-(Mabbb9)),

・(Mabba1) hydrogen atom,

・(Mabba2) C_{1-6} alkyl,

・(Mabba3) aryl and

・(Mabba4) aralkyl (said alkyl, aryl and aralkyl are optionally substituted by 1 to 3 substituents selected from the following <Mabbaa1>-<Mabbaa4>),

・・<Mabbaa1> halogen atom,

・・<Mabbaa2> carboxyl,

・・<Mabbaa3> (C_{1-6} alkoxy)carbonyl and

・・<Mabbaa4> C_{1-6} alkylsulfonyl;

・(Mabbb1) single bond,

・(Mabbb2) -CO-,

・(Mabbb3) $-CO_2-$,

・(Mabbb4) -OCO-,

・(Mabbb5) $-CONR^{41c}-$,

・(Mabbb6) $-NR^{41c}CO-$,

・(Mabbb7) $-SO_2-$,

・(Mabbb8) $-SO_2NR^{41c}-$ and

・(Mabbb9) $-NR^{41c}SO_2-$ (R^{41c} is hydrogen atom or C_{1-6} alkyl);

X^{4a} is selected from the following [Lba1]-[Lba3], [Lba8], [Lba11]-[Lba13], [Lba16]-[Lba19] and [Lba21],

[Lba1] -O-,

[Lba2] -S-,

[Lba3] -CO-,

[Lba8] $-SO_2-$,

[Lba11] $-NR^{41a}-$,

[Lba12] $-CONR^{41a}-$,

[Lba13] $-NR^{41a}CO-$,

[Lba16] $-SO_2NR^{41a}-$,

[Lba17] $-NR^{41a}SO_2-$,

[Lba18] $-OCONR^{41a}-$,

[Lba19] $-NR^{41a}CO_2-$ and

[Lba21] $-NR^{41a}CONR^{41d}-$

(R^{41a} and R^{41d} are the same or different and each is hydrogen atom

or C_{1-6} alkyl);

R^{4b} is selected from the following [La1], [La2], [La5] and [La6],

[La1] hydrogen atom,

[La2] C_{1-6} alkyl,

[La5] aryl and

[La6] aralkyl

(said alkyl, aryl and aralkyl are optionally substituted by 1 to 3 substituents selected from the following <Lab1>, <Lab2>, <Lab7>, <Lab8>, <Lab12>-<Lab17>, <Lab31> and <Lab32>);

•<Lab1> halogen atom,

•<Lab2> C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from C_{1-6} alkoxy, $-SO_2-C_{1-6}$ alkyl, $-SO_2$-aryl, $-NHSO_2-C_{1-6}$ alkyl and $-NHSO_2$-halo-C_{1-6} alkyl),

•<Lab7> hydroxyl,

•<Lab8> C_{1-6} alkoxy,

•<Lab12> nitro,

•<Lab13> amino,

•<Lab14> cyano,

•<Lab15> carboxyl,

•<Lab16> (C_{1-6} alkoxy)carbonyl,

•<Lab17> C_{1-6} alkylsulfonyl,

•<Lab31> $-SO_2NR^{41f}R^{41g}$ and

•<Lab32> $-NR^{41f}SO_2R^{41h}$

(R^{41f}, R^{41g} are the same or different and each is hydrogen atom or C_{1-6} alkyl and R^{41h} is C_{1-6} alkyl);

X^{4b} is selected from the following [Maa1]-[Maa6], [Maa9], [Maa12]-[Maa16] and [Maa19]-[Maa21],

[Maa1] single bond,

[Maa2] -O-,

[Maa3] -S-,

[Maa4] -CO-,

[Maa5] $-CO_2-$,

[Maa6] -OCO-,

[Maa9] $-SO_2-$,

[Maa12] $-NR^{41b}-$,

[Maa13] $-CONR^{41b}-$,

[Maa14] $-NR^{41b}CO-$,

[Maa15] $-NR^{41b}CO_2-$,

[Maa16] $-OCONR^{41b}-$,

[Maa19] $-SO_2NR^{41b}-$,

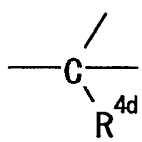
[Maa20] $-NR^{41b}SO_2-$ and

[Maa21] $-NR^{41b}CONR^{41e}-$

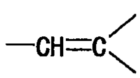
(R^{41b} and R^{41e} are the same or different and each is hydrogen atom or C_{1-6} alkyl, or show $-(CH_2)_2-$, $-(CH_2)_3-$, $-(CH_2)_4-$ or $-(CH_2)_5-$ together with R^{4b});

(A) is

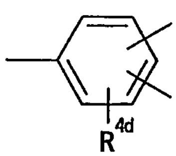
[Mab1]

 ,

[Mab2]

 or

[Mab5]



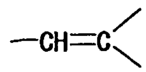
(R^{4d} is hydrogen atom or C_{1-6} alkyl),

a is an integer of 1 to 4, b is an integer of 0 to 4, c is an integer of 0 to 2 and d is an integer of 0 to 4, or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

(6) The compound of the above-mentioned (5), wherein (A) is

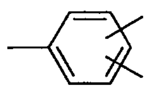
[Mab1] CH,

[Mab2]



or

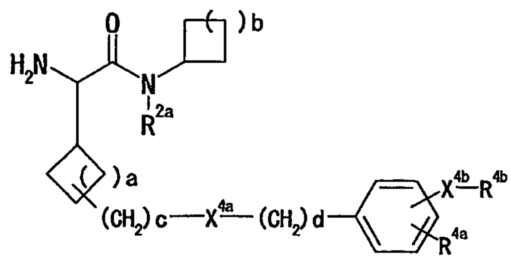
[Mab5]



,

or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

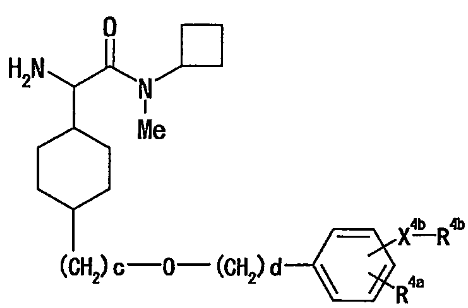
(7) A compound represented by the formula [IV]



[IV]

wherein each symbol is as defined in the above-mentioned (5), or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

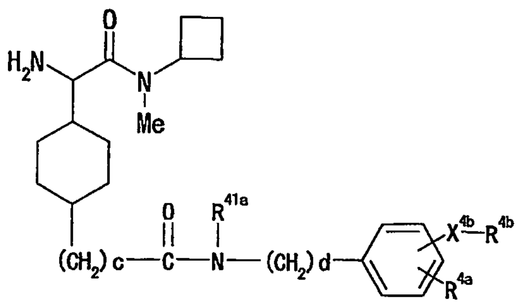
(8) A compound represented by the formula [V]



[V]

wherein each symbol is as defined in the above-mentioned (5), or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

(9) A compound represented by the formula [VI]



[VI]

wherein each symbol is as defined in the above-mentioned (5), or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

(10) A compound selected from

2-{trans-4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxymethyl}benzoic acid,

2-{trans-4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxymethyl}-5-methylbenzoic acid,

3-{trans-4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxymethyl}-5-dimethylaminobenzoic acid,

4-{trans-4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxy}-3-fluorobenzoic acid,

2-{trans-4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxymethyl}-4-methoxybenzoic acid,

2-{trans-4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxymethyl}-5-fluorobenzoic acid,

3-{trans-4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxymethyl}benzoic acid,

3-{trans-4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxy}-2-methylbenzoic acid,

3-{trans-4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxy}-5-methylbenzoic acid,

3-{trans-4-[(S)-amino-(N-cyclobutyl-N-

methylcarbamoyl)methyl]cyclohexylmethoxy}-5-dimethylaminobenzoic acid,

4-{trans-4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxy}-2-methylbenzoic acid and trans 4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexanecarboxylic acid (2-methanesulfonyl)phenylamide,

or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

(11) 2-{trans-4-[(S)-Amino-(N-cyclobutyl-N-methyl-carbamoyl)methyl]cyclohexylmethoxymethyl}benzoic acid or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

(12) 2-{trans-4-[(S)-Amino-(N-cyclobutyl-N-methyl-carbamoyl)methyl]cyclohexylmethoxymethyl}-5-methylbenzoic acid or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

(13) 3-{trans-4-[(S)-Amino-(N-cyclobutyl-N-methyl-carbamoyl)methyl]cyclohexylmethoxymethyl}-5-dimethylaminobenzoic acid or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

(14) 4-{trans-4-[(S)-Amino-(N-cyclobutyl-N-methyl-carbamoyl)methyl]cyclohexylmethoxy}-3-fluorobenzoic acid or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

(15) trans 4-[(S)-Amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexanecarboxylic acid (2-methanesulfonyl)phenylamide or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

(16) A pharmaceutical composition comprising the compound of any of the above-mentioned (2) to (15), or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof, and a pharmaceutically acceptable carrier or excipient.

(17) A drug for the treatment of diabetes, which comprises the

compound of any of the above-mentioned (2) to (15), or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

(18) A DPP-IV inhibitor, which comprises a compound of any of the above-mentioned (2) to (15), or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

(19) The pharmaceutical composition of the above-mentioned (16), which is used in combination with a different therapeutic drug for diabetes, a therapeutic drug for diabetic complication, a therapeutic drug for hyperlipidemia or an anti-obesity drug.

(20) The pharmaceutical compossition of the above-mentioned (19), wherein the different therapeutic drug for diabetes, the therapeutic drug for diabetic complication, the therapeutic drug for hyperlipidemia or the anti-obesity drug is selected from insulin preparations (injection), low-molecular insulin preparations (oral agent), sulfonylurea receptor agonists (SU drugs), short acting insulin secretagogues, α-glucosidase inhibitors, insulin sensitizers, PPARα receptor agonists, PPARγ receptor agonists/antagonists, PPARδ receptor agonists, tGLP-1 receptor agonists, glucagon receptor antagonists, glucocorticoid receptor antagonists, biguanides, SGLUT inhibitors, fructose-1,6-bisphosphatases (FBPase) inhibitors, glycogen synthase kinase 3 (GSK-3) inhibitors, phosphoenolpyruvate carboxykinase (PEPCK) inhibitors, protein tyrosine phosphatase 1B (PTPase 1B) inhibitors, SH2 domain-containing inositol phosphatase (SHIP2) inhibitors, AMP-activated protein kinase (AMPK) activators, glycogen phosphorylase (GP) inhibitors, glucokinase activators, 11β-HSD-1 inhibitors, GPR40 receptor agonists, pyruvate dehydrogenase kinase (PDHK) inhibitors, microsomal triglyceride transfer protein (MTP) inhibitors, diacylglycerol acyltransferase (DGAT) inhibitors, cholesteryl ester transfer protein (CETP) inhibitors, HMG-CoA reductase inhibitors, β3 adrenaline receptor agonists, apolipoprotein-A1 (Apo-A1) inducers, lipoprotein lipase (LPL) activators, glucose-dependent insulinotropic polypeptide (GIP)

receptor antagonists, leptin receptor agonists, bombesin receptor subtype 3 (BRS-3) agonists, perilipin inhibitors, acetyl-CoA carboxylase 1 (ACC1) inhibitors, acetyl-CoA carboxylase 2 (ACC2) inhibitors, melanocortin (MC) receptor agonists, neuropeptide Y5 (NPY5) receptor antagonists, adiponectin receptor agonists, protein kinase β (PKCβ) inhibitors, endothelial lipase inhibitors, angiotensin II receptor antagonists, aldose reductase inhibitors, angiotensin conversion enzyme (ACE) inhibitors, advanced glycation end products (AGE) inhibitors, glutamine/fructose-6-phosphate aminotransferase (GFAT) inhibitors and uncoupling protein (UCP) inducers/activators.

(21) A method for treating diabetes, which comprises administering an effective amount of the compound of any of the above-mentioned (2) to (15) or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof, to a mammal.

(22) A method for inhibiting DPP-IV, comprising using the compound of the above-mentioned (2) to (15), or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

(23) The method of the above-mentioned (21), which is used in combination with a different therapeutic drug for diabetes, a therapeutic drug for diabetic complication, a therapeutic drug for hyperlipidemia or an anti-obesity drug.

(24) The method of the above-mentioned (23), wherein the different therapeutic drug for diabetes, the therapeutic drug for diabetic complication, the therapeutic drug for hyperlipidemia or the anti-obesity drug is selected from insulin preparations (injection), low-molecular insulin preparations (oral agent), sulfonylurea receptor agonists (SU drugs), short acting insulin secretagogues, α-glucosidase inhibitors, insulin sensitizers, PPARα receptor agonists, PPARγ receptor agonists/antagonists, PPARδ receptor agonists, tGLP-1 receptor agonists, glucagon receptor antagonists, glucocorticoid receptor antagonists, biguanides, SGLUT inhibitors, fructose-1,6-bisphosphatases (FBPase) inhibitors, glycogen synthase kinase 3 (GSK-3) inhibitors, phosphoenolpyruvate

carboxykinase (PEPCK) inhibitors, protein tyrosine phosphatase 1B (PTPase 1B) inhibitors, SH2 domain-containing inositol phosphatase (SHIP2) inhibitors, AMP-activated protein kinase (AMPK) activators, glycogen phosphorylase (GP) inhibitors, glucokinase activators, 11β-HSD-1 inhibitors, GPR40 receptor agonists, pyruvate dehydrogenase kinase (PDHK) inhibitors, microsomal triglyceride transfer protein (MTP) inhibitors, diacylglycerol acyltransferase (DGAT) inhibitors, cholesteryl ester transfer protein (CETP) inhibitors, HMG-CoA reductase inhibitors, β3 adrenaline receptor agonists, apolipoprotein-A1 (Apo-A1) inducers, lipoprotein lipase (LPL) activators, glucose-dependent insulinotropic polypeptide (GIP) receptor antagonists, leptin receptor agonists, bombesin receptor subtype 3 (BRS-3) agonists, perilipin inhibitors, acetyl-CoA carboxylase 1 (ACC1) inhibitors, acetyl-CoA carboxylase 2 (ACC2) inhibitors, melanocortin (MC) receptor agonists, neuropeptide Y5 (NPY5) receptor antagonists, adiponectin receptor agonists, protein kinase β (PKCβ) inhibitors, endothelial lipase inhibitors, angiotensin II receptor antagonists, aldose reductase inhibitors, angiotensin conversion enzyme (ACE) inhibitors, advanced glycation end products (AGE) inhibitors, glutamine/fructose-6-phosphate aminotransferase (GFAT) inhibitors and uncoupling protein (UCP) inducers/activators.

(25) Use of the compound of any of the above-mentioned (2) to (15) or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof for the manufacture of a drug for the treatment of diabetes.

(26) Use of the compound of the above-mentioned (2) to (15) or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof for the manufacture of a medicament for inhibiting DPP-IV.

(27) Use of the above-mentioned (25), which is used in combination with a different therapeutic drug for diabetes, a therapeutic drug for diabetic complication, a therapeutic drug for hyperlipidemia or an anti-obesity drug.

(28) Use of the above-mentioned (27), wherein the different therapeutic drug for diabetes, the therapeutic drug for diabetic complication, the therapeutic drug for hyperlipidemia or the anti-obesity drug is selected from insulin preparations (injection), low-molecular insulin preparations (oral agent), sulfonylurea receptor agonists (SU drugs), short acting insulin secretagogues, α-glucosidase inhibitors, insulin sensitizers, PPARα receptor agonists, PPARγ receptor agonists/antagonists, PPARδ receptor agonists, tGLP-1 receptor agonists, glucagon receptor antagonists, glucocorticoid receptor antagonists, biguanides, SGLUT inhibitors, fructose-1,6-bisphosphatases (FBPase) inhibitors, glycogen synthase kinase 3 (GSK-3) inhibitors, phosphoenolpyruvate carboxykinase (PEPCK) inhibitors, protein tyrosine phosphatase 1B (PTPase 1B) inhibitors, SH2 domain-containing inositol phosphatase (SHIP2) inhibitors, AMP-activated protein kinase (AMPK) activators, glycogen phosphorylase (GP) inhibitors, glucokinase activators, 11β-HSD-1 inhibitors, GPR40 receptor agonists, pyruvate dehydrogenase kinase (PDHK) inhibitors, microsomal triglyceride transfer protein (MTP) inhibitors, diacylglycerol acyltransferase (DGAT) inhibitors, cholesteryl ester transfer protein (CETP) inhibitors, HMG-CoA reductase inhibitors, β3 adrenaline receptor agonists, apolipoprotein-A1 (Apo-A1) inducers, lipoprotein lipase (LPL) activators, glucose-dependent insulinotropic polypeptide (GIP) receptor antagonists, leptin receptor agonists, bombesin receptor subtype 3 (BRS-3) agonists, perilipin inhibitors, acetyl-CoA carboxylase 1 (ACC1) inhibitors, acetyl-CoA carboxylase 2 (ACC2) inhibitors, melanocortin (MC) receptor agonists, neuropeptide Y5 (NPY5) receptor antagonists, adiponectin receptor agonists, protein kinase β (PKC) inhibitors, endothelial lipase inhibitors, angiotensin II receptor antagonists, aldose reductase inhibitors, angiotensin conversion enzyme (ACE) inhibitors, advanced glycation end products (AGE) inhibitors, glutamine/fructose-6-phosphate aminotransferase (GFAT) inhibitors and uncoupling protein (UCP) inducers/activators.

(29) A commercial package comprising the pharmaceutical composition of any of the above-mentioned (16), (19) and (20) and a written matter associated therewith, the written matter stating that the pharmaceutical composition may or should be used for treating diabetes.

The present invention includes the following embodiments.

(30) A DPP-IV inhibitor comprising a compound of the formula [I], wherein

R^4 is selected from the following [K]-[S], or a salt thereof.

[K] hydrogen atom,

[L] C_{1-6} alkyl (alkyl is optionally substituted by 1 to 3 substituents selected from the following <L1>-<L14>),

·<L1> halogen atom,

·<L2> C_{3-12} cycloalkyl,

·<L3> hydroxyl,

·<L4> C_{1-6} alkoxy,

·<L5> C_{1-6} alkylthio,

·<L6> aryloxy,

·<L7> aralkyloxy,

·<L8> heterocyclyloxy,

·<L9> heterocyclyl-C_{1-6} alkoxy,

·<L10> nitro,

·<L11> amino,

·<L12> cyano,

·<L13> carboxyl and

·<L14> $-Y^{41}-R^{41}$ (R^{41} is selected from the following (La2) and (La4)-(La7), and Y^{41} is selected from the following (Lb1) and (Lb2)),

··(La2) C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <Laa1>-<Laa10>, <Laa16> and <Laa19>),

···<Laa1> halogen atom,

···<Laa2> C_{3-12} cycloalkyl,

···<Laa3> hydroxyl,

···<Laa4> aralkyloxy,

···<Laa5> heterocyclyloxy,

···<Laa6> heterocyclyl-C_{1-6} alkoxy,

···<Laa7> nitro,

···<Laa8> cyano,

···<Laa9> carboxyl,

···<Laa10> C_{1-6} alkoxy, aryloxy,

···<Laa16> amino and

···<Laa19> C_{1-6} alkylthio;

··(La4) C_{3-12} cycloalkyl-C_{1-6} alkyl,

··(La5) aryl,

··(La6) aralkyl and

··(La7) heterocyclyl (said aryl, aralkyl and heterocyclyl are optionally substituted by 1 to 3 substituents selected from the following <Lab1>-<Lab15>, <Lab19> and <Lab28>),

···<Lab1> halogen atom,

···<Lab2> C_{1-6} alkyl,

···<Lab3> halo-C_{1-6} alkyl,

···<Lab4> aralkyl,

···<Lab5> heterocyclyl-C_{1-6} alkyl,

···<Lab6> C_{3-12} cycloalkyl,

···<Lab7> hydroxyl,

···<Lab8> C_{1-6} alkoxy,

···<Lab9> aralkyloxy,

···<Lab10> heterocyclyloxy,

···<Lab11> heterocyclyl-C_{1-6} alkoxy,

···<Lab12> nitro,

···<Lab13> amino,

···<Lab14> cyano,

···<Lab15> carboxyl,

···<Lab19> aryloxy and

···<Lab28> C_{1-6} alkylthio;

··(Lb1) single bond and

··(Lb2) X^{41} (X^{41} is selected from the following (Lba1)-(Lba23)),

···(Lba1) $-O-$, $-OCH_2-$, $-OCH_2CH_2-$, $-CH_2O-$, $-CH_2CH_2O-$,

···(Lba2) $-S-$, $-SCH_2-$, $-SCH_2CH_2-$, $-CH_2S-$, $-CH_2CH_2S-$,

···(Lba3) $-CO-$, $-COCH_2-$, $-COCH_2CH_2-$, $-CH_2CO-$, $-CH_2CH_2CO-$,

···(Lba4) $-CO_2-$,

···(Lba5) $-OCO-$,

···(Lba6) $-OCO_2-$,

···(Lba7) $-SO-$, $-SOCH_2-$, $-SOCH_2CH_2-$, $-CH_2SO-$, $-CH_2CH_2SO-$,

···(Lba8) $-SO_2-$, $-SO_2CH_2-$, $-SO_2CH_2CH_2-$, $-CH_2SO_2-$, $-CH_2CH_2SO_2-$,

···(Lba9) $-OSO_2-$,

···(Lba10) $-SO_3-$,

···(Lba11) $-NR^{411}-$, $-NR^{411}CH_2-$, $-NR^{411}CH_2CH_2-$, $-CH_2NR^{411}-$, $-CH_2CH_2NR^{411}-$,

···(Lba12) $-CONR^{411}-$,

···(Lba13) $-NR^{411}CO-$,

···(Lba14) $-CSNR^{411}-$,

···(Lba15) $-NR^{411}CS-$,

···(Lba16) $-SO_2NR^{411}-$,

···(Lba17) $-NR^{411}SO_2-$,

···(Lba18) $-OCONR^{411}-$,

···(Lba19) $-NR^{411}CO_2-$,

···(Lba20) $-NR^{411}CONR^{412}-$,

···(Lba21) $-NR^{411}CSNR^{412}-$,

···(Lba22) $-NR^{411}SO_2NR^{412}-$ (R^{411}, R^{412} are the same or different and each is selected from the following (Lbaa1)-(Lbaa3)),

····(Lbaa1) hydrogen atom,

····(Lbaa2) C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <Lbaaa1>-<Lbaaa13>),

·····<Lbaaa1> halogen atom,

·····<Lbaaa2> C_{3-12} cycloalkyl,

·····<Lbaaa3> hydroxyl,

·····<Lbaaa4> C_{1-6} alkoxy,

·····<Lbaaa5> C_{1-6} alkylthio,

·····<Lbaaa6> aryloxy,

·····<Lbaaa7> aralkyloxy,

·····<Lbaaa8> heterocyclyloxy,

·····<Lbaaa9> heterocyclyl-C_{1-6} alkoxy,

·····<Lbaaa10> nitro,

·····<Lbaaa11> amino,

·····<Lbaaa12> cyano and

·····<Lbaaa13> carboxyl; and

····(Lbaa3) $-(CH_2)_p-$ (p is an integer of 1 to 3) formed by R^{411} and R^{412} in combination); and

···(Lba23) 4 to 7-membered divalent saturated heterocycle;

[M] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <M1>-<M18>),

·<M1> halogen atom,

·<M2> C_{1-6} alkyl,

·<M3> halo-C_{1-6} alkyl,

·<M4> aralkyl,

·<M5> heterocyclyl-C_{1-6} alkyl,

·<M6> hydroxyl,

·<M7> C_{1-6} alkoxy,

·<M8> C_{1-6} alkylthio,

·<M9> aryloxy,

·<M10> aralkyloxy,

·<M11> heterocyclyloxy,

·<M12> heterocyclyl-C_{1-6} alkoxy,

·<M13> azido,

·<M14> nitro,

·<M15> amino,

·<M16> cyano,

·<M17> carboxyl and

·<M18> $-Y^{42}-R^{41}$ (R^{41} is as defined above, and Y^{42} is selected from the following (Ma1)-(Ma12)),

··(Ma1) single bond,

··(Ma2) $-X^{41}-$,

··(Ma3) $-Z^{41}-$,

··(Ma4) $-Z^{41}-Z^{42}-$,

··(Ma5) $-X^{41}-Z^{41}-$,

··(Ma6) $-Z^{41}-X^{41}-$,

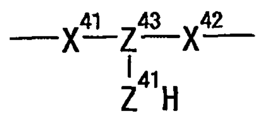
••(Ma7) $-X^{41}-Z^{41}-X^{42}-$,

••(Ma8) $-X^{41}-Z^{41}-Z^{42}-$,

••(Ma9) $-Z^{41}-X^{41}-Z^{42}-$,

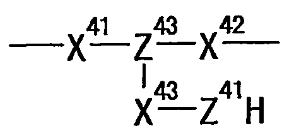
••(Ma10) $-Z^{41}-Z^{42}-X^{41}-$,

••(Ma11)



or

••(Ma12)



(X^{41} is as defined above, X^{42} and X^{43} are the same as X^{41}, Z^{41} and Z^{42} are the same or different and each is selected from the following (Mab1), (Mab3)-(Mab6) and Z^{43} is selected from the following (Mac1), (Mac3)-(Mac5)),

•••(Mab1) C_{1-6} alkylene,

•••(Mab2) C_{2-6} alkenylene (said alkylene and alkenylene is optionally substituted by 1 to 3 substituents selected from the following <Maba1>-<Maba13>),

••••<Maba1> halogen atom,

••••<Maba2> C_{3-12} cycloalkyl,

••••<Maba3> hydroxyl,

••••<Maba4> C_{1-6} alkoxy,

••••<Maba5> C_{1-6} alkylthio,

••••<Maba6> aryloxy,

••••<Maba7> aralkyloxy,

••••<Maba8> heterocyclyloxy,

••••<Maba9> heterocyclyl-C_{1-6} alkoxy,

••••<Maba10> nitro,

····<Maba11> amino,

····<Maba12> cyano and

····<Maba13> carboxyl;

···(Mab4) C_{3-12} cycloalkylene,

···(Mab5) arylene and

···(Mab6) divalent heterocycle (said cycloalkylene, arylene and heterocycle are optionally substituted by 1 to 3 substituents selected from the following <Mabb1>-<Mabb17>),

····<Mabb1> halogen atom,

····<Mabb2> C_{1-6} alkyl,

····<Mabb3> halo-C_{1-6} alkyl,

····<Mabb4> aralkyl,

····<Mabb5> heterocyclyl-C_{1-6} alkyl,

····<Mabb6> C_{3-12} cycloalkyl,

····<Mabb7> hydroxyl,

····<Mabb8> C_{1-6} alkoxy,

····<Mabb9> C_{1-6} alkylthio,

····<Mabb10> aryloxy,

····<Mabb11> aralkyloxy,

····<Mabb12> heterocyclyloxy,

····<Mabb13> heterocyclyl-C_{1-6} alkoxy,

····<Mabb14> nitro,

····<Mabb15> amino,

····<Mabb16> cyano and

····<Mabb17> carboxyl;

···(Mac1) C_{1-6} alkanetriyl (said alkanetriyl is optionally substituted by 1 to 3 substituents selected from the following <Maca1>-<Maca13>),

····<Maca1> halogen atom,

····<Maca2> C_{3-12} cycloalkyl,

····<Maca3> hydroxyl,

····<Maca4> C_{1-6} alkoxy,

····<Maca5> C_{1-6} alkylthio,

····<Maca6> aryloxy,

....<Maca7> aralkyloxy,

....<Maca8> heterocyclyloxy,

....<Maca9> heterocyclyl-C_{1-6} alkoxy,

....<Maca10> nitro,

....<Maca11> amino,

....<Maca12> cyano and

....<Maca13> carboxyl;

...(Mac3) C_{3-12} cycloalkanetriyl,

...(Mac4) arenetriyl and

...(Mac5) trivalent heterocycle (asid cycloalkanetriyl, arenetriyl and heterocycle are optionally substituted by 1 to 3 substituents selected from the following <Macb1>-<Macb17>),

....<Macb1> halogen atom,

....<Macb2> C_{1-6} alkyl,

....<Macb3> halo-C_{1-6} alkyl,

....<Macb4> aralkyl,

....<Macb5> heterocyclyl-C_{1-6} alkyl,

....<Macb6> C_{3-12} cycloalkyl,

....<Macb7> hydroxyl,

....<Macb8> C_{1-6} alkoxy,

....<Macb9> C_{1-6} alkylthio,

....<Macb10> aryloxy,

....<Macb11> aralkyloxy,

....<Macb12> heterocyclyloxy,

....<Macb13> heterocyclyl-C_{1-6} alkoxy,

....<Macb14> nitro,

....<Macb15> amino,

....<Macb16> cyano and

....<Macb17> carboxyl;

[N] aryl,

[O] aralkyl,

[P] heterocyclyl,

[Q] heterocyclyl-C_{1-6} alkyl (said aryl, aralkyl, heterocyclyl and heterocyclyl-C_{1-6} alkyl are optionally substituted by 1 to 3

substituents selected from the following <N1>-<N19>),

•<N1> halogen atom,

•<N2> C_{1-6} alkyl,

•<N3> C_{3-12} cycloalkyl,

•<N4> halo-C_{1-6} alkyl,

•<N5> aralkyl,

•<N6> heterocyclyl-C_{1-6} alkyl,

•<N7> hydroxyl,

•<N8> C_{1-6} alkoxy,

•<N9> C_{1-6} alkylthio,

•<N10> aryloxy,

•<N11> aralkyloxy,

•<N12> heterocyclyloxy,

•<N13> heterocyclyl-C_{1-6} alkoxy,

•<N14> nitro,

•<N15> amino,

•<N16> cyano,

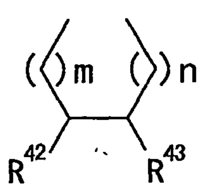
•<N17> =O,

•<N18> carboxyl and

•<N19> $-Y^{42}-R^{41}$ (R^{41} and Y^{42} are as defined above);

[R] $-Y^{41}-R^{41}$ (R^{41} and Y^{41} are as defined above), or

[S]



(R^{42} and R^{43} are each independently selected from the following (S1)-(S3) and m and n are each independently an integer of 0 to 3) formed by R^4 and R^5 in combination,

•(S1) hydrogen atom,

•(S2) $-Y^{41}-R^{44}$ (R^{44} is selected from the following (Sa1) and (Sa2) and Y^{41} is as defined above),

••(Sa1) aryl and

••(Sa2) heterocyclyl (said aryl and heterocyclyl are optionally substituted by 1 to 3 substituents selected from the following <Saa1>-<Saa17>),

•••<Saa1> halogen atom,

•••<Saa2> C_{1-6} alkyl,

•••<Saa3> halo-C_{1-6} alkyl,

•••<Saa4> aralkyl,

•••<Saa5> heterocyclyl-C_{1-6} alkyl,

•••<Saa6> C_{3-12} cycloalkyl,

•••<Saa7> hydroxyl,

•••<Saa8> C_{1-6} alkoxy,

•••<Saa9> C_{1-6} alkylthio,

•••<Saa10> aryloxy,

•••<Saa11> aralkyloxy,

•••<Saa12> heterocyclyloxy,

•••<Saa13> heterocyclyl-C_{1-6} alkoxy,

•••<Saa14> nitro,

•••<Saa15> amino,

•••<Saa16> cyano and

•••<Saa17> carboxyl;

or

•(S3) benzene ring formed by R^{42} and R^{43} together with the adjacent carbon atoms (said benzene ring is optionally substituted by 1 to 3 substituents selected from the following <Sc1>-<Sc17>),

••<Sc1> halogen atom,

••<Sc2> C_{1-6} alkyl,

••<Sc3> halo-C_{1-6} alkyl,

••<Sc4> aralkyl,

••<Sc5> heterocyclyl-C_{1-6} alkyl,

••<Sc6> C_{3-12} cycloalkyl,

••<Sc7> hydroxyl,

••<Sc8> C_{1-6} alkoxy,

••<Sc9> C_{1-6} alkylthio,

••<Sc10> aryloxy,

••<Sc11> aralkyloxy,

••<Sc12> heterocyclyloxy,

••<Sc13> heterocyclyl-C_{1-6} alkoxy,

••<Sc14> nitro,

••<Sc15> amino,

••<Sc16> cyano and

••<Sc17> carboxyl.

(31) A compound wherein, in the formula [II], $R^{4'}$ is selected from the following [K]-[M], [P], [R] and [S], or a salt thereof:

[K] hydrogen atom,

[L] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <L1>-<L14>),

•<L1> halogen atom,

•<L2> C_{3-12} cycloalkyl,

•<L3> hydroxyl,

•<L4> C_{1-6} alkoxy,

•<L5> C_{1-6} alkylthio,

•<L6> aryloxy,

•<L7> aralkyloxy,

•<L8> heterocyclyloxy,

•<L9> heterocyclyl-C_{1-6} alkoxy,

•<L10> nitro,

•<L11> amino,

•<L12> cyano,

•<L13> carboxyl and

•<L14> $-Y^{41}-R^{41'}$ ($R^{41'}$ is selected from the following (La2), (La5) and (La7), Y^{41} is as defined in the above-mentioned (30)),

••(La2) C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <Laa1>-<Laa10>, <Laa16> and <Laa19>),

•••<Laa1> halogen atom,

•••<Laa2> C_{3-12} cycloalkyl,

•••<Laa3> hydroxyl,

...<Laa4> aralkyloxy,

...<Laa5> heterocyclyloxy,

...<Laa6> heterocyclyl-C_{1-6} alkoxy,

...<Laa7> nitro,

...<Laa8> cyano,

...<Laa9> carboxyl,

...<Laa10> C_{1-6} alkoxy, aryloxy,

...<Laa16> amino and

...<Laa19> C_{1-6} alkylthio;

..(La5) aryl and

..(La7) heterocyclyl (said aryl and heterocyclyl are optionally substituted by 1 to 3 substituents selected from the following <Lab1>-<Lab15>, <Lab19> and <Lab28>),

...<Lab1> halogen atom,

...<Lab2> C_{1-6} alkyl,

...<Lab3> halo-C_{1-6} alkyl,

...<Lab4> aralkyl,

...<Lab5> heterocyclyl-C_{1-6} alkyl,

...<Lab6> C_{3-12} cycloalkyl,

...<Lab7> hydroxyl,

...<Lab8> C_{1-6} alkoxy,

...<Lab9> aralkyloxy,

...<Lab10> heterocyclyloxy,

...<Lab11> heterocyclyl-C_{1-6} alkoxy,

...<Lab12> nitro,

...<Lab13> amino,

...<Lab14> cyano,

...<Lab15> carboxyl,

...<Lab19> aryloxy and

...<Lab28> C_{1-6} alkylthio;

[M] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <M1>-<M18>),

.<M1> halogen atom,

.<M2> C_{1-6} alkyl,

•<M3> halo-C_{1-6} alkyl,

•<M4> aralkyl,

•<M5> heterocyclyl-C_{1-6} alkyl,

•<M6> hydroxyl,

•<M7> C_{1-6} alkoxy,

•<M8> C_{1-6} alkylthio,

•<M9> aryloxy,

•<M10> aralkyloxy,

•<M11> heterocyclyloxy,

•<M12> heterocyclyl-C_{1-6} alkoxy,

•<M13> azido,

•<M14> nitro,

•<M15> amino,

•<M16> cyano,

•<M17> carboxyl and

•<M18> $-Y^{42}-R^{41'}$ ($R^{41'}$ is as defined above, Y^{42} is as defined in the above-mentioned (30));

[P] 3 to 7-membered saturated heterocycle (said saturated heterocycle is optionally substituted by 1 to 3 substituents selected from the following <N1>-<N16> and <N18>),

•<N1> halogen atom,

•<N2> C_{1-6} alkyl,

•<N3> C_{3-12} cycloalkyl,

•<N4> halo-C_{1-6} alkyl,

•<N5> aralkyl,

•<N6> heterocyclyl-C_{1-6} alkyl,

•<N7> hydroxyl,

•<N8> C_{1-6} alkoxy,

•<N9> C_{1-6} alkylthio,

•<N10> aryloxy,

•<N11> aralkyloxy,

•<N12> heterocyclyloxy,

•<N13> heterocyclyl-C_{1-6} alkoxy,

•<N14> nitro,

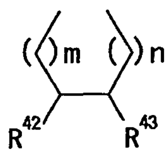
·<N15> amino,

·<N16> cyano and

·<N18> carboxyl;

[R] $-Y^{41}-R^{41'}$ ($R^{41'}$ and Y^{41} are as defined above), or

[S]



(R^{42} and R^{43} are each as defined in the above-mentioned (30) and m and n are each independently an integer of 0 to 3) formed by $R^{4'}$ and $R^{5'}$ in combination,

provided that, when R^1 and $R^{2'}$ are hydrogen atoms and $R^{3'}$ is cyclopropyl, then the combination of one of $R^{4'}$ and $R^{5'}$ being isopropyl or tert-butyl, and the other being hydrogen atom does not occur, and when R^1 and $R^{2'}$ are hydrogen atoms and $R^{3'}$ is cyclobutyl, then the combination of one of $R^{4'}$ and $R^{5'}$ being tert-butyl, and the other being hydrogen atom does not occur.

(32) The compound of the above-mentioned (31), wherein

R^1 is

[A] hydrogen atom,

[B] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <B1>-<B4>, <B10>-<B12> and <B14>),

·<B1> halogen atom,

·<B2> C_{3-12} cycloalkyl,

·<B3> hydroxyl,

·<B4> C_{1-6} alkoxy,

·<B10> nitro,

·<B11> amino,

·<B12> cyano and

·<B14> $-X^1-R^{11}$ (R^{11} and X^1 are each as defined in the above-mentioned (1));

or

[C] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <C1>, <C2>, <C6>, <C7> and <C13>-<C17>),

·<C1> halogen atom,

·<C2> C_{1-6} alkyl,

·<C6> hydroxyl,

·<C7> C_{1-6} alkoxy,

·<C13> nitro,

·<C14> amino,

·<C15> cyano,

·<C16> carboxyl and

·<C17> $-X^1-R^{11}$ (R^{11} and X^1 are as defined above);

$R^{2'}$ is

[F] hydrogen atom,

[G] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from <G1>-<G4>, <G10>-<G13> and <G16>-<G18>),

·<G1> halogen atom,

·<G2> C_{3-12} cycloalkyl,

·<G3> hydroxyl,

·<G4> C_{1-6} alkoxy,

·<G10> nitro,

·<G11> amino,

·<G12> cyano,

·<G13> amido,

·<G16> $-PO(OH)_2$,

·<G17> $-PO(O-C_{1-6}$ alkyl$)_2$ and

·<G18> $-PO(O-aryl)_2$;

or

[H] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <H1>, <H2>, <H6>, <H7>, <H13>-<H16> and <H19>-<H21>),

·<H1> halogen atom,

·<H2> C_{1-6} alkyl,

•<H6> hydroxyl,

•<H7> C_{1-6} alkoxy,

•<H13> nitro,

•<H14> amino,

•<H15> cyano,

•<H16> amido,

•<H19> $-PO(OH)_2$,

•<H20> $-PO(O-C_{1-6}\ alkyl)_2$ and

•<H21> $-PO(O-aryl)_2$;

$R^{3'}$ is

[J] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <J1>, <J2>, <J6>, <J7>, <J13>-<J16> and <J19>-<J21>),

•<J1> halogen atom,

•<J2> C_{1-6} alkyl,

•<J6> hydroxyl,

•<J7> C_{1-6} alkoxy,

•<J13> nitro,

•<J14> amino and

•<J15> cyano,

•<J16> amido,

•<J19> $-PO(OH)_2$,

•<J20> $-PO(O-C_{1-6}\ alkyl)_2$ and

•<J21> $-PO(O-aryl)_2$;

$R^{4'}$ is

[K] hydrogen atom,

[L] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <L1>-<L4> and <L10>-<L12>),

•<L1> halogen atom,

•<L2> C_{3-12} cycloalkyl,

•<L3> hydroxyl,

•<L4> C_{1-6} alkoxy,

•<L10> nitro,

·<L11> amino and

·<L12> cyano;

[M] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <M1>, <M2>, <M6>, <M7>, <M13>-<M16> and <M18>)

·<M1> halogen atom,

·<M2> C_{1-6} alkyl,

·<M6> hydroxyl,

·<M7> C_{1-6} alkoxy,

·<M13> azido,

·<M14> nitro,

·<M15> amino,

·<M16> cyano and

·<M18> $-Y^{42}-R^{41'}$ ($R^{41'}$ is as defined in the above-mentioned (31), and Y^{42} is as defined in the above-mentioned (30));

[P] 3 to 7-membered saturated heterocycle (said saturated heterocycle is optionally substituted by 1 to 3 substituents selected from the following <N1>, <N2>, <N7>, <N8>, <N14>-<N16> and <N18>),

·<N1> halogen atom,

·<N2> C_{1-6} alkyl,

·<N7> hydroxyl,

·<N8> C_{1-6} alkoxy,

·<N14> nitro,

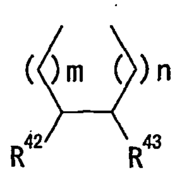
·<N15> amino,

·<N16> cyano and

·<N18> carboxyl;

or

[S]



(R^{42} and R^{43} are as defined in the above-mentioned (30) and m and n are each independently an integer of 0 to 3) formed by $R^{4'}$ and $R^{5'}$ in combination;

$R^{5'}$ is

[T] hydrogen atom,

[U] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <U1>-<U4> and <U10>-<U12>)

·<U1> halogen atom,

·<U2> C_{3-12} cycloalkyl,

·<U3> hydroxyl,

·<U4> C_{1-6} alkoxy,

·<U10> nitro,

·<U11> amino and

·<U12> cyano;

or

[V] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <V1>, <V2>, <V6>, <V7> and <V13>-<V15>),

·<V1> halogen atom,

·<V2> C_{1-6} alkyl,

·<V6> hydroxyl,

·<V7> C_{1-6} alkoxy,

·<V13> nitro,

·<V14> amino and

·<V15> cyano,

provided that, when R^1 and $R^{2'}$ are hydrogen atoms and $R^{3'}$ is cyclopropyl, then the combination of one of $R^{4'}$ and $R^{5'}$ being isopropyl or tert-butyl, and the other being hydrogen atom does not occur, and when R^1 and $R^{2'}$ are hydrogen atoms and $R^{3'}$ is cyclobutyl, then the combination of one of $R^{4'}$ and $R^{5'}$ being tert-butyl, and the other being hydrogen atom does not occur, or a salt thereof.

(33) A DPP-IV inhibitor comprising a compound of the formula [I], wherein

R^1 is

[A] hydrogen atom,

[B] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <B1>-<B14>),

·<B1> halogen atom,

·<B2> C_{3-12} cycloalkyl,

·<B3> hydroxyl,

·<B4> C_{1-6} alkoxy,

·<B5> C_{1-6} alkylthio,

·<B6> aryloxy,

·<B7> aralkyloxy,

·<B8> heteroaryloxy,

·<B9> heteroaryl-C_{1-6} alkoxy,

·<B10> nitro,

·<B11> amino,

·<B12> cyano,

·<B13> carboxyl and

·<B14> $-X^1-R^{11}$ (R^{11} is selected from the following (Ba1) and (Ba2), and X^1 is selected from the following (Bb1)-(Bb5) and (Bb13)-(Bb22)),

··(Ba1) aryl and

··(Ba2) heteroaryl (said aryl and heteroaryl are optionally substituted by 1 to 3 substituents selected from the following <Baa1>, <Baa2>, <Baa4> and <Baa7>-<Baa17>),

···<Baa1> halogen atom,

···<Baa2> C_{1-6} alkyl,

···<Baa4> C_{3-12} cycloalkyl,

···<Baa7> hydroxyl,

···<Baa8> C_{1-6} alkoxy,

···<Baa9> C_{1-6} alkylthio,

···<Baa10> aryloxy,

···<Baa11> aralkyloxy,

...<Baa12> heteroaryloxy,

...<Baa13> heteroaryl-C_{1-6} alkoxy,

...<Baa14> nitro,

...<Baa15> amino,

...<Baa16> cyano and

...<Baa17> carboxyl;

..(Bb1) single bond,

..(Bb2) -O-,

..(Bb3) -S-,

..(Bb4) -NH-,

..(Bb5) -CO-,

..(Bb13) -CONH-,

..(Bb14) -NHCO-,

..(Bb15) -CSNH-,

..(Bb16) -NHCS-,

..(Bb17) -$NHSO_2$-,

..(Bb18) -SO_2NH-,

..(Bb19) -$NHCO_2$-,

..(Bb20) -OCONH-,

..(Bb21) -NHCONH- and

..(Bb22) -NHCSNH-;

[C] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <C1>, <C2> and <C6>-<C17>),

.<C1> halogen atom,

.<C2> C_{1-6} alkyl,

.<C6> hydroxyl,

.<C7> C_{1-6} alkoxy,

.<C8> C_{1-6} alkylthio,

.<C9> aryloxy,

.<C10> aralkyloxy,

.<C11> heteroaryloxy,

.<C12> heteroaryl-C_{1-6} alkoxy,

.<C13> nitro,

•<C14> amino,

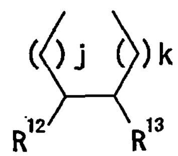
•<C15> cyano,

•<C16> carboxyl and

•<C17> $-X^1-R^{11}$ (R^{11} and X^1 are as defined above);

[D] $-X^1-R^{11}$ (R^{11} and X^1 are as defined above) or

[E]



(R^{12} and R^{13} are each independently selected from the following (E1)-(E3), and j and k are each independently an integer of 0 to 3) formed by R^1 and R^4 in combination,

•(E1) hydrogen atom,

•(E2) $-X^{12}-R^{14}$ (R^{14} is selected from the following (Ea1) and (Ea2), and X^{12} is selected from the following (Eb1)-(Eb5), (Eb13)-(Eb22) and (Eb24)),

••(Ea1) aryl and

••(Ea2) heteroaryl (said aryl and heteroaryl are optionally substituted by 1 to 3 substituents selected from the following <Eaa1>-<Eaa4>, <Eaa7>-<Eaa17>),

•••<Eaa1> halogen atom,

•••<Eaa2> C_{1-6} alkyl,

•••<Eaa3> halo-C_{1-6} alkyl,

•••<Eaa4> C_{3-12} cycloalkyl,

•••<Eaa7> hydroxyl,

•••<Eaa8> C_{1-6} alkoxy,

•••<Eaa9> C_{1-6} alkylthio,

•••<Eaa10> aryloxy,

•••<Eaa11> aralkyloxy,

•••<Eaa12> heteroaryloxy,

•••<Eaa13> heteroaryl-C_{1-6} alkoxy,

•••<Eaa14> nitro,

···<Eaa15> amino,

···<Eaa16> cyano and

···<Eaa17> carboxyl;

··(Eb1) single bond,

··(Eb2) -O-,

··(Eb3) -S-,

··(Eb4) -NH-,

··(Eb5) -CO-,

··(Eb13) -CONH-,

··(Eb14) -NHCO-,

··(Eb15) -CSNH-,

··(Eb16) -NHCS-,

··(Eb17) $-NHSO_2-$,

··(Eb18) $-SO_2NH-$,

··(Eb19) $-NHCO_2-$,

··(Eb20) -OCONH-,

··(Eb21) -NHCONH-,

··(Eb22) -NHCSNH- and

··(Eb24) 4 to 7-membered divalent saturated heterocycle;

or

·(E3) benzene ring formed by R^{12} and R^{13} together with the adjacent carbon atoms (said benzene ring is optionally substituted by 1 to 3 substituents selected from the following <Ec1>-<Ec4> and <Ec7>-<Ec17>),

··<Ec1> halogen atom,

··<Ec2> C_{1-6} alkyl,

··<Ec3> halo-C_{1-6} alkyl,

··<Ec4> C_{3-12} cycloalkyl,

··<Ec7> hydroxyl,

··<Ec8> C_{1-6} alkoxy,

··<Ec9> C_{1-6} alkylthio,

··<Ec10> aryloxy,

··<Ec11> aralkyloxy,

··<Ec12> heteroaryloxy,

··<Ec13> heteroaryl-C_{1-6} alkoxy,

··<Ec14> nitro,

··<Ec15> amino,

··<Ec16> cyano and

··<Ec17> carboxyl;

R^2 is

[F] hydrogen atom,

[G] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <G1>-<G16>)

·<G1> halogen atom,

·<G2> C_{3-12} cycloalkyl,

·<G3> hydroxyl,

·<G4> C_{1-6} alkoxy,

·<G5> C_{1-6} alkylthio,

·<G6> aryloxy,

·<G7> aralkyloxy,

·<G8> heteroaryloxy,

·<G9> heteroaryl-C_{1-6} alkoxy,

·<G10> nitro,

·<G11> amino,

·<G12> cyano,

·<G13> amido,

·<G14> =O,

·<G15> carboxyl and

·<G16> $-PO(OH)_2$;

or

[H] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <H1>, <H2> and <H6>-<H19>),

·<H1> halogen atom,

·<H2> C_{1-6} alkyl,

·<H6> hydroxyl,

·<H7> C_{1-6} alkoxy,

·<H8> C_{1-6} alkylthio,

•<H9> aryloxy,

•<H10> aralkyloxy,

•<H11> heteroaryloxy,

•<H12> heteroaryl-C_{1-6} alkoxy,

•<H13> nitro,

•<H14> amino,

•<H15> cyano,

•<H16> amido,

•<H17> =O,

•<H18> carboxyl and

•<H19> -PO(OH)$_2$;

R^3 is

[I] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <I1>-<I16>),

•<I1> halogen atom,

•<I2> C_{3-12} cycloalkyl,

•<I3> hydroxyl,

•<I4> C_{1-6} alkoxy,

•<I5> C_{1-6} alkylthio,

•<I6> aryloxy,

•<I7> aralkyloxy,

•<I8> heteroaryloxy,

•<I9> heteroaryl-C_{1-6} alkoxy,

•<I10> nitro,

•<I11> amino,

•<I12> cyano,

•<I13> amido,

•<I14> =O,

•<I15> carboxyl and

•<I16> -PO(OH)$_2$;

or

[J] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <J1>, <J2> and <J6>-<J19>),

•<J1> halogen atom,

•<J2> C_{1-6} alkyl,

•<J6> hydroxyl,

•<J7> C_{1-6} alkoxy,

•<J8> C_{1-6} alkylthio,

•<J9> aryloxy,

•<J10> aralkyloxy,

•<J11> heteroaryloxy,

•<J12> heteroaryl-C_{1-6} alkoxy,

•<J13> nitro,

•<J14> amino,

•<J15> cyano,

•<J16> amido,

•<J17> =O,

•<J18> carboxyl and

•<J19> $-PO(OH)_2$;

R^4 and R^5 are each independently,

[K] hydrogen atom,

[L] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <L1>-<L14>),

•<L1> halogen atom,

•<L2> C_{3-12} cycloalkyl,

•<L3> hydroxyl,

•<L4> C_{1-6} alkoxy,

•<L5> C_{1-6} alkylthio,

•<L6> aryloxy,

•<L7> aralkyloxy,

•<L8> heteroaryloxy,

•<L9> heteroaryl-C_{1-6} alkoxy,

•<L10> nitro,

•<L11> amino,

•<L12> cyano,

•<L13> carboxyl and

•<L14> $-Y^{41}-R^{41}$ (R^{41} is selected from the following (La5) and (La7),

and Y^{41} is selected from the following (Lb1) and (Lb2))

••(La5) aryl and

••(La7) heteroaryl (said aryl and heteroaryl are optionally substituted by 1 to 3 substituents selected from the following <Lab1>, <Lab2>, <Lab6>-<Lab15>, <Lab19> and <Lab28>),

•••<Lab1> halogen atom,

•••<Lab2> C_{1-6} alkyl,

•••<Lab6> C_{3-12} cycloalkyl,

•••<Lab7> hydroxyl,

•••<Lab8> C_{1-6} alkoxy,

•••<Lab9> aralkyloxy,

•••<Lab10> heteroaryloxy,

•••<Lab11> heteroaryl-C_{1-6} alkoxy,

•••<Lab12> nitro,

•••<Lab13> amino,

•••<Lab14> cyano,

•••<Lab15> carboxyl,

•••<Lab19> aryloxy and

•••<Lab28> C_{1-6} alkylthio;

••(Lb1) single bond and

••(Lb2) X^{41} (X^{41} is selected from the following (Lba1)-(Lba3) and (Lba11)-(Lba21)),

•••(Lba1) -O-,

•••(Lba2) -S-,

•••(Lba3) -CO-,

•••(Lba11) $-NR^{411}-$,

•••(Lba12) $-CONR^{411}-$,

•••(Lba13) $-NR^{411}CO-$,

•••(Lba14) $-CSNR^{411}-$,

•••(Lba15) $-NR^{411}CS-$,

•••(Lba16) $-SO_2NR^{411}-$,

•••(Lba17) $-NR^{411}SO_2-$,

•••(Lba18) $-OCONR^{411}-$,

•••(Lba19) $-NR^{411}CO_2-$,

•••(Lba20) $-NR^{411}CONR^{412}-$ and

•••(Lba21) $-NR^{411}CSNR^{412}-$ (R^{411}, R^{412} are each hydrogen atom);

[M] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <M1>, <M2>, <M6>-<M12> and <M14>-<M18>),

•<M1> halogen atom,

•<M2> C_{1-6} alkyl,

•<M6> hydroxyl,

•<M7> C_{1-6} alkoxy,

•<M8> C_{1-6} alkylthio,

•<M9> aryloxy,

•<M10> aralkyloxy,

•<M11> heteroaryloxy,

•<M12> heteroaryl-C_{1-6} alkoxy,

•<M14> nitro,

•<M15> amino,

•<M16> cyano,

•<M17> carboxyl and

•<M18> $-Y^{42}-R^{41}$ (R^{41} is as defined above, and Y^{42} is selected from the following (Ma1) and (Ma2)),

••(Ma1) single bond and

••(Ma2) X^{41} (X^{41} are as defined above);

[N] aryl,

[O] aralkyl,

[P] 3 to 7-membered saturated heterocycle or heteroaryl,

[Q] heteroaryl-C_{1-6} alkyl (said aryl, aralkyl, saturated heterocycle, heteroaryl and heteroaryl-C_{1-6} alkyl are optionally substituted by 1 to 3 substituents selected from the following <N1>-<N3>, <N7>-<N16> and <N18>),

•<N1> halogen atom,

•<N2> C_{1-6} alkyl,

•<N3> C_{3-12} cycloalkyl,

•<N7> hydroxyl,

•<N8> C_{1-6} alkoxy,

·<N9> C_{1-6} alkylthio,

·<N10> aryloxy,

·<N11> aralkyloxy,

·<N12> heteroaryloxy,

·<N13> heteroaryl-C_{1-6} alkoxy,

·<N14> nitro,

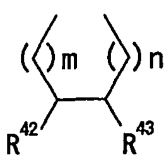
·<N15> amino,

·<N16> cyano and

·<N18> carboxyl;

[R] R^{41}-Y^{41}- (R^{41} and Y^{41} are as defined above), or

[S]



(R^{42} and R^{43} are each independently selected from the following (S1)-(S3), and m and n are each independently an integer of 0 to 3) formed by R^4 and R^5 in combination,

·(S1) hydrogen atom,

·(S2) -Y^{411}-R^{44} (R^{44} is selected from the following (Sa1) and (Sa2), and Y^{411} is selected from the following (Lb1) and (Lb2))

··(Sa1) aryl and

··(Sa2) heteroaryl (said aryl and heteroaryl are optionally substituted by 1 to 3 substituents selected from the following <Saa1>-<Saa3> and <Saa6>-<Saa17>),

···<Saa1> halogen atom,

···<Saa2> C_{1-6} alkyl,

···<Saa3> halo-C_{1-6} alkyl,

···<Saa6> C_{3-12} cycloalkyl,

···<Saa7> hydroxyl,

···<Saa8> C_{1-6} alkoxy,

···<Saa9> C_{1-6} alkylthio,

···<Saa10> aryloxy,

•••<Saa11> aralkyloxy,

•••<Saa12> heteroaryloxy,

•••<Saa13> heteroaryl-C_{1-6} alkoxy,

•••<Saa14> nitro,

•••<Saa15> amino,

•••<Saa16> cyano and

•••<Saa17> carboxyl;

••(Lb1) single bond and

••(Lb2) X^{411} (X^{411} is selected from the following (Lba1)-(Lba3), (Lba11)-(Lba21) and (Lba23)),

•••(Lba1) -O-,

•••(Lba2) -S-,

•••(Lba3) -CO-,

•••(Lba11) $-NR^{411}-$,

•••(Lba12) $-CONR^{411}-$,

•••(Lba13) $-NR^{411}CO-$,

•••(Lba14) $-CSNR^{411}-$,

•••(Lba15) $-NR^{411}CS-$,

•••(Lba16) $-SO_2NR^{411}-$,

•••(Lba17) $-NR^{411}SO_2-$,

•••(Lba18) $-OCONR^{411}-$,

•••(Lba19) $-NR^{411}CO_2-$,

•••(Lba20) $-NR^{411}CONR^{412}-$,

•••(Lba21) $-NR^{411}CSNR^{412}-$ (R^{411}, R^{412} are each hydrogen atom), and

•••(Lba23) 4 to 7-membered divalent saturated heterocycle;

or

•(S3) benzene ring formed by R^{42} and R^{43} together with the adjacent carbon atoms (said benzene ring is optionally substituted by 1 to 3 substituents selected from the following <Sc1>-<Sc3> and <Sc6>-<Sc17>),

••<Sc1> halogen atom,

••<Sc2> C_{1-6} alkyl,

••<Sc3> halo-C_{1-6} alkyl,

••<Sc6> C_{3-12} cycloalkyl,

••<Sc7> hydroxyl,

••<Sc8> C_{1-6} alkoxy,

••<Sc9> C_{1-6} alkylthio,

••<Sc10> aryloxy,

••<Sc11> aralkyloxy,

••<Sc12> heteroaryloxy,

••<Sc13> heteroaryl-C_{1-6} alkoxy,

••<Sc14> nitro,

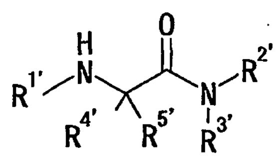
••<Sc15> amino,

••<Sc16> cyano and

••<Sc17> carboxyl,

or a salt thereof.

(34) A compound represented by the formula [IV]



[IV]

wherein $R^{1'}$ is the following [A]-[E]:

[A] hydrogen atom,

[B] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <B1>-<B12> and <B14>),

•<B1> halogen atom,

•<B2> C_{3-12} cycloalkyl,

•<B3> hydroxyl,

•<B4> C_{1-6} alkoxy,

•<B5> C_{1-6} alkylthio,

•<B6> aryloxy,

•<B7> aralkyloxy,

•<B8> heteroaryloxy,

•<B9> heteroaryl-C_{1-6} alkoxy,

•<B10> nitro,

•<B11> amino,

•<B12> cyano and

•<B14> $-X^1-R^{11}$ (R^{11} is selected from the following (Ba1) and (Ba2), and X^1 is selected from the following (Bb1)-(Bb5) and (Bb13)-(Bb22)),

••(Ba1) aryl and

••(Ba2) heteroaryl (said aryl and heteroaryl are optionally substituted by 1 to 3 substituents selected from the following <Baa1>, <Baa2>,<Baa4> and <Baa7>-<Baa17>)

•••<Baa1> halogen atom,

•••<Baa2> C_{1-6} alkyl,

•••<Baa4> C_{3-12} cycloalkyl,

•••<Baa7> hydroxyl,

•••<Baa8> C_{1-6} alkoxy,

•••<Baa9> C_{1-6} alkylthio,

•••<Baa10> aryloxy,

•••<Baa11> aralkyloxy,

•••<Baa12> heteroaryloxy,

•••<Baa13> heteroaryl-C_{1-6} alkoxy,

•••<Baa14> nitro,

•••<Baa15> amino,

•••<Baa16> cyano and

•••<Baa17> carboxyl;

••(Bb1) single bond,

••(Bb2) -O-,

••(Bb3) -S-,

••(Bb4) -NH-,

••(Bb5) -CO-,

••(Bb13) -CONH-,

••(Bb14) -NHCO-,

••(Bb15) -CSNH-,

••(Bb16) -NHCS-,

••(Bb17) $-NHSO_2-$,

••(Bb18) $-SO_2NH-$,

••(Bb19) $-NHCO_2-$,

••(Bb20) -OCONH-,

••(Bb21) -NHCONH- and

••(Bb22) -NHCSNH-;

[C] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <C1>, <C2>, <C6>-<C15> and <C17>),

•<C1> halogen atom,

•<C2> C_{1-6} alkyl,

•<C6> hydroxyl,

•<C7> C_{1-6} alkoxy,

•<C8> C_{1-6} alkylthio,

•<C9> aryloxy,

•<C10> aralkyloxy,

•<C11> heteroaryloxy,

•<C12> heteroaryl-C_{1-6} alkoxy,

•<C13> nitro,

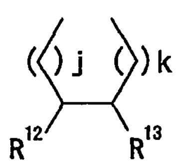
•<C14> amino,

•<C15> cyano and

•<C17> $-X^1-R^{11}$ (R^{11} and X^1 are as defined above);

[D] $-X^1-R^{11}$ (R^{11} and X^1 are as defined above) or

[E]



(R^{12} and R^{13} are each independently selected from the following (E1)-(E3), and j and k are each independently an integer of 0 to 3) formed by $R^{1'}$ and $R^{4'}$ in combination,

•(E1) hydrogen atom,

•(E2) $-X^{12}-R^{14}$ (R^{14} is selected from the following (Ea1) and (Ea2), and X^{12} is selected from the following (Eb1)-(Eb5), (Eb13)-(Eb22) and (Eb24)),

••(Ea1) aryl and

••(Ea2) heteroaryl (said aryl and heteroaryl are optionally substituted by 1 to 3 substituents selected from the following <Eaa1>-<Eaa4> and <Eaa7>-<Eaa17>),

•••<Eaa1> halogen atom,

•••<Eaa2> C_{1-6} alkyl,

•••<Eaa3> halo-C_{1-6} alkyl,

•••<Eaa4> C_{3-12} cycloalkyl,

•••<Eaa7> hydroxyl,

•••<Eaa8> C_{1-6} alkoxy,

•••<Eaa9> C_{1-6} alkylthio,

•••<Eaa10> aryloxy,

•••<Eaa11> aralkyloxy,

•••<Eaa12> heteroaryloxy,

•••<Eaa13> heteroaryl-C_{1-6} alkoxy,

•••<Eaa14> nitro,

•••<Eaa15> amino,

•••<Eaa16> cyano and

•••<Eaa17> carboxyl;

••(Eb1) single bond,

••(Eb2) -O-,

••(Eb3) -S-,

••(Eb4) -NH-,

••(Eb5) -CO-,

••(Eb13) -CONH-,

••(Eb14) -NHCO-,

••(Eb15) -CSNH-,

••(Eb16) -NHCS-,

••(Eb17) $-NHSO_2-$,

••(Eb18) $-SO_2NH-$,

••(Eb19) $-NHCO_2-$,

••(Eb20) -OCONH-,

••(Eb21) -NHCONH-,

••(Eb22) -NHCSNH- and

••(Eb24) 4 to 7-membered divalent saturated heterocycle;

or

• (E3) benzene ring formed by R^{12} and R^{13} together with the adjacent carbon atoms (said benzene ring is optionally substituted by 1 to 3 substituents selected from the following <Ec1>-<Ec4> and <Ec7>-<Ec17>),

••<Ec1> halogen atom,

••<Ec2> C_{1-6} alkyl,

••<Ec3> halo-C_{1-6} alkyl,

••<Ec4> C_{3-12} cycloalkyl,

••<Ec7> hydroxyl,

••<Ec8> C_{1-6} alkoxy,

••<Ec9> C_{1-6} alkylthio,

••<Ec10> aryloxy,

••<Ec11> aralkyloxy,

••<Ec12> heteroaryloxy,

••<Ec13> heteroaryl-C_{1-6} alkoxy,

••<Ec14> nitro,

••<Ec15> amino,

••<Ec16> cyano and

••<Ec17> carboxyl;

$R^{2'}$ is selected from the following [F]-[H]:

[F] hydrogen atom,

[G] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <G1>-<G12>),

•<G1> halogen atom,

•<G2> C_{3-12} cycloalkyl,

•<G3> hydroxyl,

•<G4> C_{1-6} alkoxy,

•<G5> C_{1-6} alkylthio,

•<G6> aryloxy,

•<G7> aralkyloxy,

•<G8> heteroaryloxy,

•<G9> heteroaryl-C_{1-6} alkoxy,

•<G10> nitro,

•<G11> amino and

•<G12> cyano;

and

[H] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <H1>, <H2> and <H6>–<H15>),

•<H1> halogen atom,

•<H2> C_{1-6} alkyl,

•<H6> hydroxyl,

•<H7> C_{1-6} alkoxy,

•<H8> C_{1-6} alkylthio,

•<H9> aryloxy,

•<H10> aralkyloxy,

•<H11> heteroaryloxy,

•<H12> heteroaryl-C_{1-6} alkoxy,

•<H13> nitro,

•<H14> amino and

•<H15> cyano;

$R^{3'}$ is the following [J]:

[J] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <J1>, <J2> and <J6>–<J15>),

•<J1> halogen atom,

•<J2> C_{1-6} alkyl,

•<J6> hydroxyl,

•<J7> C_{1-6} alkoxy,

•<J8> C_{1-6} alkylthio,

•<J9> aryloxy,

•<J10> aralkyloxy,

•<J11> heteroaryloxy,

•<J12> heteroaryl-C_{1-6} alkoxy,

•<J13> nitro,

•<J14> amino and

•<J15> cyano;

R^{4}' and R^{5}' are each independently selected from the following [K]-[M], [P], [R] and [S]:

[K] hydrogen atom,

[L] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <L1>-<L12> and <L14>),

·<L1> halogen atom,

·<L2> C_{3-12} cycloalkyl,

·<L3> hydroxyl,

·<L4> C_{1-6} alkoxy,

·<L5> C_{1-6} alkylthio,

·<L6> aryloxy,

·<L7> aralkyloxy,

·<L8> heteroaryloxy,

·<L9> heteroaryl-C_{1-6} alkoxy,

·<L10> nitro,

·<L11> amino,

·<L12> cyano and

·<L14> $-Y^{41}-R^{41}$' (R^{41}' is selected from the following (La5) and (La7), and Y^{41} is selected from (Lb1) and (Lb2)),

··(La5) aryl and

··(La7) heteroaryl (said aryl and heteroaryl are optionally substituted by 1 to 3 substituents selected from the following <Lab1>, <Lab2>, <Lab6>-<Lab15>, <Lab19> and <Lab28>),

···<Lab1> halogen atom,

···<Lab2> C_{1-6} alkyl,

···<Lab6> C_{3-12} cycloalkyl,

···<Lab7> hydroxyl,

···<Lab8> C_{1-6} alkoxy,

···<Lab9> aralkyloxy,

···<Lab10> heteroaryloxy,

···<Lab11> heteroaryl-C_{1-6} alkoxy,

···<Lab12> nitro,

···<Lab13> amino,

···<Lab14> cyano,

•••<Lab15> carboxyl,

•••<Lab19> aryloxy and

•••<Lab28> C_{1-6} alkylthio;

••(Lb1) single bond and

••(Lb2) X^{41} (X^{41} is selected from the following (Lba1)-(Lba3) and (Lba11)-(Lba21)),

•••(Lba1) -O-,

•••(Lba2) -S-,

•••(Lba3) -CO-,

•••(Lba11) $-NR^{411}-$,

•••(Lba12) $-CONR^{411}-$,

•••(Lba13) $-NR^{411}CO-$,

•••(Lba14) $-CSNR^{411}-$,

•••(Lba15) $-NR^{411}CS-$,

•••(Lba16) $-SO_2NR^{411}-$,

•••(Lba17) $-NR^{411}SO_2-$,

•••(Lba18) $-OCONR^{411}-$,

•••(Lba19) $-NR^{411}CO_2-$,

•••(Lba20) $-NR^{411}CONR^{412}-$ and

•••(Lba21) $-NR^{411}CSNR^{412}-$ (R^{411}, R^{412} are each hydrogen atom);

[M] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <M1>, <M2>, <M6>-<M12>, <M14>-<M16> and <M18>),

•<M1> halogen atom,

•<M2> C_{1-6} alkyl,

•<M6> hydroxyl,

•<M7> C_{1-6} alkoxy,

•<M8> C_{1-6} alkylthio,

•<M9> aryloxy,

•<M10> aralkyloxy,

•<M11> heteroaryloxy,

•<M12> heteroaryl-C_{1-6} alkoxy,

•<M14> nitro,

•<M15> amino,

·<M16> cyano and

·<M18> $-Y^{42}-R^{41'}$ ($R^{41'}$ is as defined above, and Y^{42} is as defined for Y^{41});

[P] 3 to 7-membered saturated heterocycle (said saturated heterocycle is optionally substituted by 1 to 3 substituents selected from the following <N1>-<N3>, <N7>-<N16> and <N18>),

·<N1> halogen atom,

·<N2> C_{1-6} alkyl,

·<N3> C_{3-12} cycloalkyl,

·<N7> hydroxyl,

·<N8> C_{1-6} alkoxy,

·<N9> C_{1-6} alkylthio,

·<N10> aryloxy,

·<N11> aralkyloxy,

·<N12> heteroaryloxy,

·<N13> heteroaryl-C_{1-6} alkoxy,

·<N14> nitro,

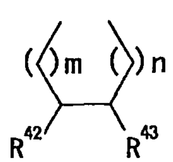
·<N15> amino,

·<N16> cyano and

·<N18> carboxyl;

[R] $-Y^{41}-R^{41'}$ ($R^{41'}$ and Y^{41} are as defined above); or

[S]



(R^{42} and R^{43} are each independently selected from the following (S1)-(S3), and m and n are each independently an integer of 0 to 3) formed by $R^{4'}$ and $R^{5'}$ in combination,

·(S1) hydrogen atom,

·(S2) $-Y^{411}-R^{44}$ (R^{44} is selected from the following (Sa1) and (Sa2), and Y^{411} is selected from the following (Lb1) and (Lb2)),

··(Sa1) aryl and

··(Sa2) heteroaryl (said aryl and heteroaryl are optionally substituted by 1 to 3 substituents selected from the following <Saa1>-<Saa3> and <Saa6>-<Saa17>),

···<Saa1> halogen atom,

···<Saa2> C_{1-6} alkyl,

···<Saa3> halo-C_{1-6} alkyl,

···<Saa6> C_{3-12} cycloalkyl,

···<Saa7> hydroxyl,

···<Saa8> C_{1-6} alkoxy,

···<Saa9> C_{1-6} alkylthio,

···<Saa10> aryloxy,

···<Saa11> aralkyloxy,

···<Saa12> heteroaryloxy,

···<Saa13> heteroaryl-C_{1-6} alkoxy,

···<Saa14> nitro,

···<Saa15> amino,

···<Saa16> cyano and

···<Saa17> carboxyl

··(Lb1) single bond and

··(Lb2) X^{411} (X^{411} is selected from the following (Lba1)-(Lba3), (Lba11)-(Lba21) and (Lba23)),

···(Lba1) -O-,

···(Lba2) -S-,

···(Lba3) -CO-,

···(Lba11) $-NR^{411}-$,

···(Lba12) $-CONR^{411}-$,

···(Lba13) $-NR^{411}CO-$,

···(Lba14) $-CSNR^{411}-$,

···(Lba15) $-NR^{411}CS-$,

···(Lba16) $-SO_2NR^{411}-$,

···(Lba17) $-NR^{411}SO_2-$,

···(Lba18) $-OCONR^{411}-$,

···(Lba19) $-NR^{411}CO_2-$,

···(Lba20) $-NR^{411}CONR^{412}-$,

···(Lba21) $-NR^{411}CSNR^{412}-$ (R^{411}, R^{412} are each hydrogen atom)

and

···(Lba23) 4 to 7-membered divalent saturated heterocycle;

or

·(S3) benzene ring formed by R^{42} and R^{43} together with the adjacent carbon atoms (said benzene ring is optionally substituted by 1 to 3 substituents selected from the following <Sc1>-<Sc3> and <Sc6>-<Sc17>),

··<Sc1> halogen atom,

··<Sc2> C_{1-6} alkyl,

··<Sc3> halo-C_{1-6} alkyl,

··<Sc6> C_{3-12} cycloalkyl,

··<Sc7> hydroxyl,

··<Sc8> C_{1-6} alkoxy,

··<Sc9> C_{1-6} alkylthio,

··<Sc10> aryloxy,

··<Sc11> aralkyloxy,

··<Sc12> heteroaryloxy,

··<Sc13> heteroaryl-C_{1-6} alkoxy,

··<Sc14> nitro,

··<Sc15> amino,

··<Sc16> cyano and

··<Sc17> carboxyl;

provided that, when $R^{1'}$ and $R^{2'}$ are hydrogen atoms and $R^{3'}$ is cyclopropyl, then the combination of one of $R^{4'}$ and $R^{5'}$ being isopropyl or tert-butyl, and the other being hydrogen atom does not occur, and when $R^{1'}$ and $R^{2'}$ are hydrogen atoms and $R^{3'}$ is cyclobutyl, then the combination of one of $R^{4'}$ and $R^{5'}$ being tert-butyl, and the other being hydrogen atom does not occur, or a salt thereof.

(35) A compound of the formula [IV],

wherein

$R^{1'}$ is

[A] hydrogen atom,

[B] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <B1>-<B4>, <B10>-<B12> and <B14>),

·<B1> halogen atom,

·<B2> C_{3-12} cycloalkyl,

·<B3> hydroxyl,

·<B4> C_{1-6} alkoxy,

·<B10> nitro,

·<B11> amino,

·<B12> cyano and

·<B14> $-X^1-R^{11}$ (R^{11} is selected from the following (Ba1) and (Ba2), X^1 is selected from the following (Bb1)-(Bb5) and (Bb13)-(Bb22))

··(Ba1) aryl and

··(Ba2) heteroaryl (said aryl and heteroaryl are optionally substituted by 1 to 3 substituents selected from the following <Baa1>, <Baa2>, <Baa4>, <Baa7>, <Baa8> and <Baa14>-<Baa17>)

···<Baa1> halogen atom,

···<Baa2> C_{1-6} alkyl,

···<Baa4> C_{3-12} cycloalkyl,

···<Baa7> hydroxyl,

···<Baa8> C_{1-6} alkoxy,

···<Baa14> nitro,

···<Baa15> amino,

···<Baa16> cyano and

···<Baa17> carboxyl;

··(Bb1) single bond,

··(Bb2) -O-,

··(Bb3) -S-,

··(Bb4) -NH-,

··(Bb5) -CO-,

··(Bb13) -CONH-,

··(Bb14) -NHCO-,

··(Bb15) -CSNH-,

··(Bb16) -NHCS-,

··(Bb17) $-NHSO_2-$,

··(Bb18) $-SO_2NH-$,

··(Bb19) $-NHCO_2-$,

··(Bb20) -OCONH-,

··(Bb21) -NHCONH- and

··(Bb22) -NHCSNH-;

[C] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <C1>, <C2>, <C6>, <C7>, <C13>-<C15> and <C17>),

·<C1> halogen atom,

·<C2> C_{1-6} alkyl,

·<C6> hydroxyl,

·<C7> C_{1-6} alkoxy,

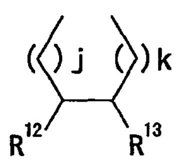
·<C13> nitro,

·<C14> amino,

·<C15> cyano and

·<C17> $-X^1-R^{11}$ (R^{11} and X^1 are as defined above); or

[E]



(R^{12} and R^{13} are each independently selected from the following (E1)-(E3), and j and k are each independently an integer of 0 to 3) formed by $R^{1'}$ and $R^{4'}$ in combination,

·(E1) hydrogen atom,

·(E2) $-X^{12}-R^{14}$ (R^{14} is selected from the following (Ea1) and (Ea2), and X^{12} is selected from the following (Eb1)-(Eb5), (Eb13)-(Eb22) and (Eb24)),

··(Ea1) aryl and

··(Ea2) heteroaryl (said aryl and heteroaryl are optionally substituted by 1 to 3 substituents selected from the following <Eaa1>-<Eaa4>, <Eaa7>, <Eaa8> and <Eaa14>-<Eaa17>),

···<Eaa1> halogen atom,

···<Eaa2> C_{1-6} alkyl,

···<Eaa3> halo-C_{1-6} alkyl,

···<Eaa4> C_{3-12} cycloalkyl,

···<Eaa7> hydroxyl,

···<Eaa8> C_{1-6} alkoxy,

···<Eaa14> nitro,

···<Eaa15> amino,

···<Eaa16> cyano and

···<Eaa17> carboxyl;

··(Eb1) single bond,

··(Eb2) -O-,

··(Eb3) -S-,

··(Eb4) -NH-,

··(Eb5) -CO-,

··(Eb13) -CONH-,

··(Eb14) -NHCO-,

··(Eb15) -CSNH-,

··(Eb16) -NHCS-,

··(Eb17) -$NHSO_2$-,

··(Eb18) -SO_2NH-,

··(Eb19) -$NHCO_2$-,

··(Eb20) -OCONH-,

··(Eb21) -NHCONH-,

··(Eb22) -NHCSNH- and

··(Eb24) 4 to 7-membered divalent saturated heterocycle;

or

·(E3) benzene ring formed by R^{12} and R^{13} together with the adjacent carbon atoms (said benzene ring is optionally substituted by 1 to 3 substituents selected from the following <Ec1>-<Ec4>, <Ec7>, <Ec8> and <Ec14>-<Ec17>),

··<Ec1> halogen atom,

··<Ec2> C_{1-6} alkyl,

··<Ec3> halo-C_{1-6} alkyl,

••<Ec4> C_{3-12} cycloalkyl,

••<Ec7> hydroxyl,

••<Ec8> C_{1-6} alkoxy,

••<Ec14> nitro,

••<Ec15> amino,

••<Ec16> cyano and

••<Ec17> carboxyl;

$R^{2\prime}$ is

[F] hydrogen atom,

[G] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from <G1>-<G4> and <G10>-<G12>),

•<G1> halogen atom,

•<G2> C_{3-12} cycloalkyl,

•<G3> hydroxyl,

•<G4> C_{1-6} alkoxy,

•<G10> nitro,

•<G11> amino and

•<G12> cyano; or

[H] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <H1>, <H2>, <H6>, <H7> and <H13>-<H15>),

•<H1> halogen atom,

•<H2> C_{1-6} alkyl,

•<H6> hydroxyl,

•<H7> C_{1-6} alkoxy,

•<H13> nitro,

•<H14> amino and

•<H15> cyano;

$R^{3\prime}$ is

[J] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <J1>, <J2>, <J6>, <J7> and <J13>-<J15>),

•<J1> halogen atom,

•<J2> C_{1-6} alkyl,

·<J6> hydroxyl,

·<J7> C_{1-6} alkoxy,

·<J13> nitro,

·<J14> amino and

·<J15> cyano;

$R^{4'}$ and $R^{5'}$ are each independently

[K] hydrogen atom,

[L] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <L1>-<L4> and <L10>-<L12>)

·<L1> halogen atom,

·<L2> C_{3-12} cycloalkyl,

·<L3> hydroxyl,

·<L4> C_{1-6} alkoxy,

·<L10> nitro,

·<L11> amino and

·<L12> cyano;

[M] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <M1>, <M2>, <M6>, <M7> and <M14>-<M16>),

·<M1> halogen atom,

·<M2> C_{1-6} alkyl,

·<M6> hydroxyl,

·<M7> C_{1-6} alkoxy,

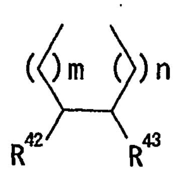
·<M14> nitro,

·<M15> amino and

·<M16> cyano;

or

[S]



. (R^{42} and R^{43} are each independently selected from the following (S1)-(S3), and m and n are each independently an integer of 0 to 3) formed by $R^{4'}$ and $R^{5'}$ in combination,

·(S1) hydrogen atom,

·(S2) $-Y^{411}-R^{44}$ (R^{44} is selected from the following (Sa1) and (Sa2), and Y^{411} is selected from the following (Lb1) and (Lb2)),

··(Sa1) aryl and

··(Sa2) heteroaryl (said aryl and heteroaryl are optionally substituted by 1 to 3 substituents selected from the following <Saa1>-<Saa3>, <Saa6>-<Saa8> and <Saa14>-<Saa17>),

···<Saa1> halogen atom,

···<Saa2> C_{1-6} alkyl,

···<Saa3> halo-C_{1-6} alkyl,

···<Saa6> C_{3-12} cycloalkyl,

···<Saa7> hydroxyl,

···<Saa8> C_{1-6} alkoxy,

···<Saa14> nitro,

···<Saa15> amino,

···<Saa16> cyano and

···<Saa17> carboxyl

··(Lb1) single bond and

··(Lb2) X^{411} (X^{411} is selected from the following (Lba1)-(Lba3), (Lba11)-(Lba21) and (Lba23)),

···(Lba1) -O-,

···(Lba2) -S-,

···(Lba3) -CO-,

···(Lba11) $-NR^{411}-$,

···(Lba12) $-CONR^{411}-$,

···(Lba13) $-NR^{411}CO-$,

···(Lba14) $-CSNR^{411}-$,

···(Lba15) $-NR^{411}CS-$,

···(Lba16) $-SO_2NR^{411}-$,

···(Lba17) $-NR^{411}SO_2-$,

···(Lba18) $-OCONR^{411}-$,

···(Lba19) $-NR^{411}CO_2-$,

···(Lba20) $-NR^{411}CONR^{412}-$,

···(Lba21) $-NR^{411}CSNR^{412}-$ (R^{411}, R^{412} are each hydrogen atom) and

···(Lba23) 4 to 7-membered divalent saturated heterocycle; or

·(S3) benzene ring formed by R^{42} and R^{43} together with the adjacent carbon atoms (said benzene ring is optionally substituted by 1 to 3 substituents selected from the following <Sc1>-<Sc3>, <Sc6>-<Sc8> and <Sc14>-<Sc17>),

··<Sc1> halogen atom,

··<Sc2> C_{1-6} alkyl,

··<Sc3> halo-C_{1-6} alkyl,

··<Sc6> C_{3-12} cycloalkyl,

··<Sc7> hydroxyl,

··<Sc8> C_{1-6} alkoxy,

··<Sc14> nitro,

··<Sc15> amino,

··<Sc16> cyano and

··<Sc17> carboxyl;

provided that, when $R^{1'}$ and $R^{2'}$ are hydrogen atoms and $R^{3'}$ is cyclopropyl, then the combination of one of $R^{4'}$ and $R^{5'}$ being isopropyl or tert-butyl, and the other being hydrogen atom does not occur, and when $R^{1'}$ and $R^{2'}$ are hydrogen atoms and $R^{3'}$ is cyclobutyl, then the combination of one of $R^{4'}$ and $R^{5'}$ being tert-butyl, and the other being hydrogen atom does not occur, or a salt thereof.

The compound of the present invention and a salt thereof encompasses a prodrug and a solvate thereof.

In the compounds [I] of the present invention, R^1 is preferably hydrogen atom, C_{1-6} alkyl or C_{3-12} cycloalkyl, more preferably hydrogen atom, C_{1-4} alkyl, C_{3-6} cycloalkyl or adamantyl, particularly preferably hydrogen atom.

R^2 is preferably hydrogen atom, C_{1-6} alkyl or C_{3-12} cycloalkyl, particularly preferably C_{1-4} alkyl.

R^3 is preferably C_{1-6} alkyl or C_{3-12} cycloalkyl, particularly

preferably C_{3-5} cycloalkyl.

R^4 is preferably hydrogen atom, C_{1-6} alkyl or C_{3-12} cycloalkyl (cycloalkyl is preferably further substituted by $-Y^{42}-R^{41}$), particularly preferably substituted C_{3-12} cycloalkyl.

R^5 is preferably hydrogen atom, C_{1-6} alkyl or C_{3-12} cycloalkyl, particularly preferably hydrogen atom.

Of R^1, R^4 and R^5, at least one is preferably a group other than hydrogen atom, and the group is preferably C_{1-4} alkyl, C_{3-6} cycloalkyl or adamantyl.

The form of the compound of the present invention is a compound *per se*, a prodrug of the compound, a salt of the compound, a salt of a prodrug of the compound, a solvate of the compound, a solvate of a salt of the compound, a solvate of a prodrug of the compound or a solvate of a salt of a prodrug of the compound, preferably a compound *per se*, a salt of the compound, a solvate of the compound, or a solvate of a salt of the compound, particularly preferably a compound *per se* or a salt of the compound.

The definition of the terms used in the present specification are as follows.

The "C_{1-6} alkyl" means a straight chain or branched chain alkyl having 1 to 6 carbon atoms, such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, pentyl, isopentyl, tert-pentyl, hexyl and the like, with preference given to C_{1-4} alkyl selected from methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl and tert-butyl.

The "halogen atom" is fluorine atom, chlorine atom, bromine atom or iodine atom. Preferred are fluorine atom, chlorine atom and bromine atom and particularly preferred is fluorine atom.

The "C_{3-12} cycloalkyl" means cyclic alkyl having 3 to 12 carbon atoms and may be a fused ring. For example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, adamantyl and the like can be mentioned, with preference given to cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and adamantyl.

The "C_{3-12} cycloalkyl C_{1-6} alkyl" means a group wherein the

aforementioned "C_{1-6} alkyl" is substituted by the aforementioned "C_{3-12} cycloalkyl", such as cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, cyclohexylmethyl, cycloheptylmethyl, adamantylmethyl, cyclopropylethyl, cyclobutylethyl, cyclopentylethyl, cyclohexylethyl, cycloheptylethyl, adamantylethyl and the like.

The "C_{1-6} alkoxy" used alone or in a compound word means a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms, such as methoxy, ethoxy, propoxy, isopropoxy, butoxy, sec-butoxy, tert-butoxy, pentyloxy, tert-pentyloxy or hexyloxy and the like, with preference given to C_{1-4} alkoxy selected from methoxy, ethoxy, propoxy, isopropoxy, butoxy, sec-butoxy and tert-butoxy.

The "C_{1-6} alkylthio" means a straight chain or branched chain alkylthio having 1 to 6 carbon atoms, such as methylthio, ethylthio, propylthio, isopropylthio, butylthio, sec-butylthio, tert-butylthio, pentylthio, tert-pentylthio, hexylthio and the like, with preference given to C_{1-4} alkylthio selected from methylthio, ethylthio, propylthio, isopropylthio, butylthio, sec-butylthio and tert-butylthio.

The "C_{1-6} alkylene" means a straight chain or branched chain alkylene having 1 to 6 carbon atoms, such as methylene, ethylene, trimethylene, propylene, tetramethylene, pentamethylene, hexamethylene, ethane-1,1-diyl, 1-methylethane-1,1-diyl and the like, with preference given to C_{1-4}alkylene such as methylene, ethylene, trimethylene, propylene, tetramethylene, ethane-1,1-diyl, 1-methylethane-1,1-diyl and the like.

The "C_{2-6} alkenylene" is a straight chain or branched chain alkenylene having 2 to 6 carbon atoms, such as $-CH=CH-$, $-CH=CH-CH_2-$, $-CH_2-CH=CH-$, $-C(CH_3)=CH-CH_2-$, $-CH=CH-CH_2-CH_2-$, $-CH_2-CH=CH-CH_2-$, $-CH_2-CH_2-CH=CH-$, $-CH=C(CH_3)-CH_2-$, pentenylene, hexenylene and the like, preferably C_{2-4} alkenylene such as $-CH=CH-$, $-CH=CH-CH_2-$, $-CH_2-CH=CH-$, $-C(CH_3)=CH-CH_2-$, $-CH=CH-CH_2-CH_2-$, $-CH_2-CH=CH-CH_2-$, $-CH_2-CH_2-CH=CH-$, $-CH=C(CH_3)-CH_2-$ and the like.

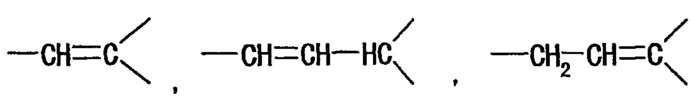
The "C_{2-6} alkynylene" is a straight chain or branched chain

alkynylene having 2 to 6 carbon atoms, such as ethynylene, 1-propyn-1,3-diyl and the like, with preference given to C_{2-4} alkynylene.

The "C_{3-12} cycloalkylene" is a cyclic alkylene having 3 to 12 carbon atoms and may be a fused ring. For example, cyclopropylene, cyclobutylene, cyclopentylene, cyclohexylene, cycloheptylene, adamantanediyl and the like can be mentioned, with preference given to cyclopropylene, cyclobutylene, cyclopentylene, cyclohexylene and adamantanediyl.

The "C_{1-6} alkanetriyl" is a straight chain or branched chain alkanetriyl having 1 to 6 carbon atoms, such as methanetriyl, ethane-1,1,2-triyl, ethane-1,1,1-triyl, propane-1,1,3-triyl, propane-1,2,3-triyl, 1-methylethane-1,1,2-triyl, propane-1,1,1-triyl, butane-1,1,4-triyl, butane-1,2,4-triyl, butane-1,1,1-triyl, pentane-1,3,5-triyl, hexane-1,3,6-triyl and the like, with preference given to C_{1-4}alkanetriyl.

The "C_{2-6} alkenetriyl" is a straight chain or branched chain alkenetriyl having 2 to 6 carbon atoms, such as



and the like, with preference given to C_{2-4} alkenetriyl.

The "C_{3-12} cycloalkanetriyl" is a cyclic alkanetriyl having 3 to 12 carbon atoms and may be a fused ring. For example, cyclopropanetriyl, cyclobutanetriyl, cyclopentanetriyl, cyclohexanetriyl, cycloheptaneriyl, adamantanetriyl and the like can be mentioned, with preference given to cyclopropanetriyl, cyclobutanetriyl, cyclopentanetriyl, cyclohexanetriyl and adamantanetriyl.

The "aryl" is an aromatic hydrocarbon group having 6 to 12 carbon atoms, and may be partially saturated. For example, phenyl, biphenyl, indenyl, naphthyl and the like can be mentioned. Preferred are phenyl and naphthyl, and particularly preferred is

phenyl. The position of binding of aryl and the position of substituent, when a substituent is present, are not particularly limited as long as they are chemically acceptable.

The "arylene" is a divalent aromatic hydrocarbon group having 6 to 12 carbon atoms and may be partially saturated. For example, phenylene, biphenyldiyl, naphthalenediyl and the like can be mentioned. Preferred are phenylene and naphthalenediyl, and particularly preferred phenylene. The position of binding of arylene and the position of substituent, when a substituent is present, are not particularly limited as long as they are chemically acceptable.

The "arenetriyl" is a trivalent aromatic hydrocarbon group having 6 to 12 carbon atoms, and may be partially saturated. For example, benzenetriyl, biphenyltriyl, naphthalenetriyl and the like can be mentioned. Preferred are benzenetriyl and naphthalenetriyl, and particularly preferred is benzenetriyl. The position of binding of arenetriyl and the position of substituent, when a substituent is present, are not particularly limited as long as they are chemically acceptable.

The "aryloxy" is a group wherein the aforementioned "aryl" is bonded via an oxygen atom. For example, phenyloxy, biphenyloxy, indenyloxy, naphthyloxy and the like can be mentioned. Preferred are phenyloxy and naphthyloxy and particularly preferred is phenyloxy. When the aryloxy has a substituent, the position of substituent is not particularly limited as long as it is chemically acceptable.

The "aralkyl" is a group wherein the aforementioned "C_{1-6}alkyl" is substituted by the aforementioned "aryl". For example, benzyl, benzhydryl, trityl, phenethyl, 3-phenylpropyl, 2-phenylpropyl, 4-phenylbutyl, indenylmethyl, naphthylmethyl, 2-naphthylethyl, 4-biphenylmethyl, 3-(4-biphenyl)propyl, 2,3-dihydroindenylmethyl, 1,2,3,4-tetrahydronaphthylmethyl and the like can be mentioned, with preference given to benzyl and phenethyl. When the aralkyl has a substituent, the position of

substituent is not particularly limited as long as it is chemically acceptable.

The "aralkyloxy" is a group wherein the aforementioned "C_{1-6}alkoxy" is substituted by the aforementioned "aryl". For example, benzyloxy, benzhydryloxy, trityloxy, phenethyloxy, 3-phenylpropoxy, 2-phenylpropoxy, 4-phenylbutoxy, indenylmethoxy, naphthylmethoxy, 2-naphthylethoxy, 4-biphenylmethoxy, 3-(4-biphenyl)propoxy, 2,3-dihydroindenylmethoxy, 1,2,3,4-tetrahydronaphthylmethoxy and the like can be mentioned, with preference given to benzyloxy and phenethyloxy.

The "heteroaryl" used alone or in a compound word means a 5- or 6-membered unsaturated ring group having 1 to 3 hetero atoms selected from nitrogen atom, oxygen atom and sulfur atom in the ring, and may be a fused ring with a benzene ring or other heterocycle. As the heteroaryl, for example, pyrrolyl, furyl, thienyl, imidazolyl, oxazolyl, thiazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, indolyl, benzofuryl, benzothienyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, pyridyl, pyrimidinyl, pyridazinyl, pyrazinyl, quinolyl, isoquinolyl and the like can be mentioned, with preference given to benzofuryl, benzothienyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, pyridyl and quinolyl. The position of binding of heteroaryl and the position of substituent, when a substituent is present, are not particularly limited as long as they are chemically acceptable.

The "heteroaryloxy" is a group wherein the aforementioned "heteroaryl" is bonded via oxygen atom, such as pyrrolyloxy, furyloxy, thienyloxy, imidazolyloxy, oxazolyloxy, thiazolyloxy, pyrazolyloxy, isoxazolyloxy, isothiazolyloxy, oxadiazolyloxy, triazolyloxy, indolyloxy, tetrazolyloxy, benzofuryloxy, benzothienyloxy, benzimidazolyloxy, benzoxazolyloxy, benzothiazolyloxy, pyridyloxy, pyrimidinyloxy, pyridazinyloxy, pyrazinyloxy, quinolyloxy, isoquinolyloxy and the like, with preference given to benzofuryloxy, benzothienyloxy,

benzimidazolyloxy, benzoxazolyloxy, benzothiazolyloxy, pyridyloxy and quinolyloxy. The position of binding of heteroaryloxy and the position of substituent, when a substituent is present, are not particularly limited as long as they are chemically acceptable.

The "heteroaryl-C_{1-6} alkyl" is a group wherein the aforementioned "C_{1-6} alkyl" is substituted by the aforementioned "heteroaryl". For example, pyrrolylmethyl, pyrrolylethyl, furylmethyl, furylethyl, imidazolylmethyl, imidazolylethyl, oxazolylmethyl, oxazolylethyl, thiazolylmethyl, thiazolylethyl, pyrazolylmethyl, pyrazolylethyl, isoxazolylmethyl, isoxazolylethyl, isothiazolylmethyl, isothiazolylethyl, oxadiazolylmethyl, oxadiazolylethyl, triazolylmethyl, triazolylethyl, tetrazolylmethyl, tetrazolylethyl, indolylmethyl, indolylethyl, benzofurylmethyl, benzofurylethyl, benzothienylmethyl, benzothienylethyl, benzimidazolylmethyl, benzimidazolylethyl, benzoxazolylmethyl, benzoxazolylethyl, benzothiazolylmethyl, benzothiazolylethyl, pyridylmethyl, pyridylethyl, pyrimidinylmethyl, pyrimidinylethyl, pyridazinylmethyl, pyridazinylethyl, pyrazinylmethyl, pyrazinylethyl, quinolylmethyl, quinolylethyl, isoquinolylmethyl, isoquinolylethyl and the like can be mentioned.

The "heteroaryl-C_{1-6} alkoxy" is a group wherein the aforementioned "C_{1-6} alkoxy" is substituted by the aforementioned "heteroaryl". For example, pyrrolylmethoxy, pyrrolylethoxy, furylmethoxy, furylethoxy, imidazolylmethoxy, imidazolylethoxy, oxazolylmethoxy, oxazolylethoxy, thiazolylmethoxy, thiazolylethoxy, pyrazolylmethoxy, pyrazolylethoxy, isoxazolylmethoxy, isoxazolylethoxy, isothiazolylmethoxy, isothiazolylethoxy, oxadiazolylmethoxy, oxadiazolylethoxy, triazolylmethoxy, triazolylethoxy, tetrazolylmethoxy, tetrazolylethoxy, indolylmethoxy, indolylethoxy, benzofurylmethoxy, benzofurylethoxy, benzothienylmethoxy, benzothienylethoxy, benzimidazolylmethoxy, benzimidazolylethoxy, benzoxazolylmethoxy, benzoxazolylethoxy, benzothiazolylmethoxy, benzothiazolylethoxy, pyridylmethoxy,

pyridylethoxy, pyrimidinylmethoxy, pyrimidinylethoxy, pyridazinylmethoxy, pyridazinylethoxy, pyrazinylmethoxy, pyrazinylethoxy, quinolylmethoxy, quinolylethoxy, isoquinolylmethoxy, isoquinolylethoxy and the like can be mentioned.

The "halo-C_{1-6} alkyl" is a haloalkyl wherein the aforementioned "C_{1-6} alkyl" is substituted by the aforementioned "one or more halogen atoms", wherein the position of substitution of the halogen atom is not particularly limited as long as it is chemically acceptable. As the "halo-C_{1-6} alkyl", for example, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, bromomethyl, dibromomethyl, tribromomethyl, iodomethyl, diiodomethyl, triiodomethyl, 2-fluoroethyl, 2,2-difluoroethyl, 2,2,2-trifluoroethyl, 2-chloroethyl, 2,2-dichloroethyl, 2,2,2-trichloroethyl, 2-bromomethyl, 2,2-dibromomethyl, 2,2,2-tribromomethyl, 3-chloropropyl or 4-chlorobutyl and the like can be mentioned, with preference given to halo-C_{1-2} alkyl selected from trifluoromethyl and 2,2,2-trichloroethyl.

The "3- to 7-membered saturated heterocycle" is a ring having 1 to 3 hetero atoms selected from nitrogen atom, oxygen atom and sulfur atom. For example, aziridine, azetidine, pyrrolidine, piperidine and hexahydroazepine and the like having one nitrogen atom as the hetero atom, and oxazolidine, isoxazolidine, thiazolidine, isothiazolidine, imidazolidine, morpholine, thiomorpholine, piperazine, tetrahydrooxazepine, tetrahydrothiazepine, hexahydrodiazepine and the like, which further have oxygen atom, sulfur atom and/or nitrogen atom as hetero atom(s), can be mentioned. The position of binding of heterocycle and the position of substituent, when a substituent is present, are not particularly limited as long as they are chemically acceptable.

The "4 to 7-membered saturated heterocycle" is a ring having 1 to 3 hetero atoms selected from nitrogen atom, oxygen atom and

sulfur atom. For example, azetidine, pyrrolidine, piperidine and hexahydroazepine and the like having one nitrogen atom as a hetero atom, and oxazolidine, thiazolidine, imidazolidine, morpholine, thiomorpholine, piperazine, tetrahydrooxazepine, tetrahydrothiazepine, hexahydrodiazepine and the like, which further have oxygen atom, sulfur atom and/or nitrogen atom as hetero atom(s), can be mentioned. The position of binding of heterocycle is not particularly limited as long as it is chemically acceptable.

The "heterocycle" is a ring having 1 to 3 hetero atoms selected from nitrogen atom, oxygen atom and sulfur atom, may be saturated or unsaturated, and may be a fused ring with a carbon ring, which is preferably 3- to 12-membered, more preferably 4- to 10-membered heterocycle.

As a monocyclic saturated heterocycle, a 3- to 7-membered saturated heterocycle having 1 to 3 hetero atoms selected from nitrogen atom, oxygen atom and sulfur atom can be mentioned. For example, a 3- to 7-membered (preferably 5- or 6-membered) saturated heterocycle having 1 to 3 nitrogen atoms (e.g., aziridine, azetidine, pyrrolidine, imidazolidine, pyrazolidine, piperidine, piperazine, hexahydroazepine, hexahydrodiazepine and the like), a 3- to 7-membered (preferably 5 or 6-membered) saturated heterocycle having 1 or 2 nitrogen atoms and one hetero atom selected from oxygen atom and sulfur atom (e.g., oxazolidine, thiazolidine, morpholine, thiomorpholine, tetrahydrooxazepine, tetrahydrothiazepine and the like), and a 3- to 7-membered (preferably 5- or 6-membered) saturated heterocycle having 1 or 2 hetero atoms selected from oxygen atom and sulfur atom (e.g., tetrahydrofuran, 1,3-dioxolane, 1,4-dioxane, tetrahydropyran, tetrahydrothiophene and the like) can be mentioned.

As the monocyclic saturated heterocycle, preferred is a 5- or 6-membered saturated heterocycle having 1 to 3 hetero atoms selected from nitrogen atom, oxygen atom and sulfur atom, more preferred are pyrrolidine, pyrazolidine, piperidine, imidazolidine,

morpholine, thiomorpholine, piperazine and the like.

As a monocyclic unsaturated heterocycle, a 3- to 7-membered unsaturated heterocycle having 1 to 3 hetero atoms selected from nitrogen atom, oxygen atom and sulfur atom can be mentioned. For example, a 3- to 7-membered (preferably 5- or 6-membered) unsaturated heterocycle having 1 to 3 nitrogen atoms (e.g., pyrrole, imidazole, pyrazole, triazole, tetrazole, pyridine, pyrimidine, pyridazine, pyrazine, triazine, pyrroline, imidazoline, pyrazoline and the like), a 3- to 7-membered (preferably 5- or 6-membered) unsaturated heterocycle having 1 or 2 nitrogen atoms and one hetero atom selected from oxygen atom and sulfur atom (e.g., oxazole, thiazole, isoxazole, isothiazole, oxadiazole, thiadiazole, oxazoline, thiazoline and the like), and a 3- to 7-membered (preferably 5 or 6-membered) unsaturated heterocycle having 1 or 2 hetero atoms selected from oxygen atom and sulfur atom (e.g., furan, thiophene and the like) can be mentioned.

As the monocyclic unsaturated heterocycle, preferred is a 5- or 6-membered aromatic heterocycle having 1 to 3 hetero atoms selected from nitrogen atom, oxygen atom and sulfur atom, more preferred are imidazole, thiazole, oxazole, tetrazole, pyridine, pyrimidine, pyrazine and the like.

As a fused heterocycle, a 8- to 12-membered saturated or unsaturated fused heterocycle having 1 to 3 hetero atoms selected from nitrogen atom, oxygen atom and sulfur atom can be mentioned. It may be a fused ring of a saturated or unsaturated heterocycle and a saturated or unsaturated carbon ring such as a benzene ring, a cyclopentane ring, a cyclohexane ring and the like, or a fused ring of saturated or unsaturated heterocycles. For example, a 8- to 12-membered (preferably 9- or 10-membered) saturated or unsaturated fused heterocycle having 1 to 3 nitrogen atoms (e.g., indole, isoindole, benzimidazole, benzotriazole, indazole, indolizine, quinoline, isoquinoline, quinazoline, cinnoline, quinoxaline, phthalazine, quinolizine, naphthyridine, pyrazolopyridine, pyrazolopyrimidine, imidazopyridine, indoline,

isoindoline, 2,3- dihydrobenzimidazole, 1,2,3,4-tetrahydroquinoline, 1,2,3,4-tetrahydroisoquinoline, 4,5,6,7-tetrahydroindole, 4,5,6,7-tetrahydroisoindole, 4,5,6,7-tetrahydrobenzimidazole and the like), a 8- to 12-membered (preferably 9- or 10-membered) saturated or unsaturated fused heterocycle having 1 or 2 nitrogen atoms and one hetero atom selected from oxygen atom and sulfur atom (e.g., benzoxazole, benzothiazole, 2,3-dihydrobenzoxazole, 2,3-dihydrobenzothiazole, 4,5,6,7-tetrahydrobenzoxazole, 4,5,6,7-tetrahydrobenzothiazole and the like), a 8- to 12-membered (preferably 9- or 10-membered) saturated or unsaturated fused heterocycle having 1 or 2 hetero atoms selected from oxygen atom and sulfur atom (e.g., benzofuran, benzothiophene, 2,3-dihydrobenzofuran, 2,3-dihydrobenzothiophene, 4,5,6,7-tetrahydrobenzofuran, 4,5,6,7-tetrahydrobenzothiophene, chroman, isochroman and the like) can be mentioned.

As the fused heterocycle, preferred is a 9- or 10-membered saturated or unsaturated fused heterocycle having 1 to 3 hetero atoms selected from nitrogen atom, oxygen atom and sulfur atom, and more preferred are benzofuran, benzothiophene, benzimidazole, benzoxazole, benzothiazole, quinoline, 3a,4,5,6,7,7a-hexahydrobenzothiazole, 3a,4,5,6,7,7a-hexahydrobenzoxazole, octahydrobenzoxazole, octahydrobenzothiazole and the like.

The "heterocyclyl" is preferably the aforementioned "heteroaryl", and more preferably benzofuryl, benzothienyl, benzoimidazolyl, benzoxazolyl, benzothiazolyl, pyridyl or quinolyl.

The "divalent heterocycle" is the aforementioned "heterocycle" having two bonds, and the "trivalent heterocycle" is the aforementioned "heterocycle" having three bonds.

The position of binding of heterocycle and the position of substituent, when a substituent is present, are not particularly limited as long as they are chemically acceptable.

The "heterocyclyl-C_{1-6} alkyl" is a group wherein the aforementioned "C_{1-6} alkyl" is substituted by the aforementioned "heterocyclyl", and, for example, those exemplified as the

aforementioned "heteroaryl-C_{1-6} alkyl" can be mentioned. The "heterocyclyl-C_{1-6} alkyl" is preferably the aforementioned "heteroaryl-C_{1-6} alkyl".

The "heterocyclyl-C_{1-6} alkoxy" is a group wherein the aforementioned "C_{1-6} alkoxy" is substituted by the aforementioned "heterocyclyl". For example, those exemplified as the aforementioned "heteroaryl-C_{1-6} alkoxy" can be mentioned. The "heterocyclyl-C_{1-6} alkoxy" is preferably the aforementioned "heteroaryl-C_{1-6} alkoxy".

The "heterocyclyloxy" is a group wherein the aforementioned "heterocyclyl" is bonded via oxygen atom. For example, those exemplified as the aforementioned "heteroaryloxy" can be mentioned. The "heterocyclyloxy" is preferably the aforementioned "heteroaryloxy".

The "amido" is a group represented by -NHCO-R^{21} (R^{21} is hydrogen atom, C_{1-6} alkyl or aryl). For example, formamido, acetamido, propaneamido, butaneamido, pentaneamido, hexaneamido, benzamido and the like can be mentioned.

A "prodrug" of a compound means a group chemically or metabolically decomposed and a derivative of the compound of the present invention that shows pharmaceutical activity after hydrolysis or solvolysis, or decomposition under physiological conditions. An ester of carboxylic acid and/or phosphoric acid of the compound [I] of the present invention can be a prodrug, and can be convered to carboxylic acid and/or phosphoric acid in living organisms.

A "pharmaceutically acceptable salt" of the compound or prodrug includes, but not limited to, inorganic acid addition salts such as hydrochloride, hydrobromide, sulfate, phosphate or nitrate and the like; organic acid addition salts such as acetate, propionate, succinate, glycolate, lactate, malate, oxalate, tartrate, citrate, maleate, fumarate, methanesulfonate, benzenesulfonate, p-toluenesulfonate, ascorbate and the like; amino acid addition salts such as aspartate, glutamate and the

like; salts with inorganic base such as sodium, potassium, calcium, magnesium, zinc and the like; salts with organic base such as methylamine, dimethylamine, ethylamine, diethylamine, triethylamine, triethanolamine, tris(hydroxymethylamino)methane, dicyclohexylamine, ethylenediamine, guanidine, meglumine, 2-aminoethanol and the like; and salts with amino acid such as aspartic acid, glutamic acid, arginine, histidine, lysin and the like.

The present invention encompasses a solvate. As used herein, a "solvate" of a compound or a prodrug or a salt thereof means, in a solid state of crystal, amorphous form and the like or a solution, one wherein the compound of the present invention is bound with a solvent molecule of water, alcohol and the like, by a relatively weak bond of van der Waals force, electrostatic interaction, hydrogen bond, charge-transfer bond, coordinate bond and the like. In some cases, the solvate may be one wherein a solvent is taken into a solid state such as a water-containing product, an alcohol-containing product and the like. As the "solvate" of the compound, preferred is a hydrate.

As the "therapeutic drug for diabetes, therapeutic drug for diabetic complication, therapeutic drug for hyperlipidemia or anti-obesity drug", insulin preparation (injection), low-molecular insulin preparation (oral agent), sulfonylurea receptor agonist (SU drugs), rapid acting insulin secretion promoter (e.g., nateglide), α-glucosidase inhibitor, insulin sensitivity enhancer, PPARα receptor agonist, PPARγ receptor agonist/antagonist, PPARδ receptor agonist, tGLP-1 receptor agonist, glucagon receptor antagonist, glucocorticoid receptor antagonist, biguanide, SGLUT inhibitor, fructose-1,6-bisphosphatases (FBPase) inhibitor, glycogen synthase kinase 3 (GSK-3) inhibitor, phosphoenolpyruvate carboxykinase (PEPCK) inhibitor, protein tyrosine phosphatase 1B (PTPase 1B) inhibitor, SH2 domain-containing inositol phosphatase (SHIP2) inhibitor, AMP-activated protein kinase (AMPK) activator, glycogen phosphorylase (GP) inhibitor, glucokinase activator, 11β-

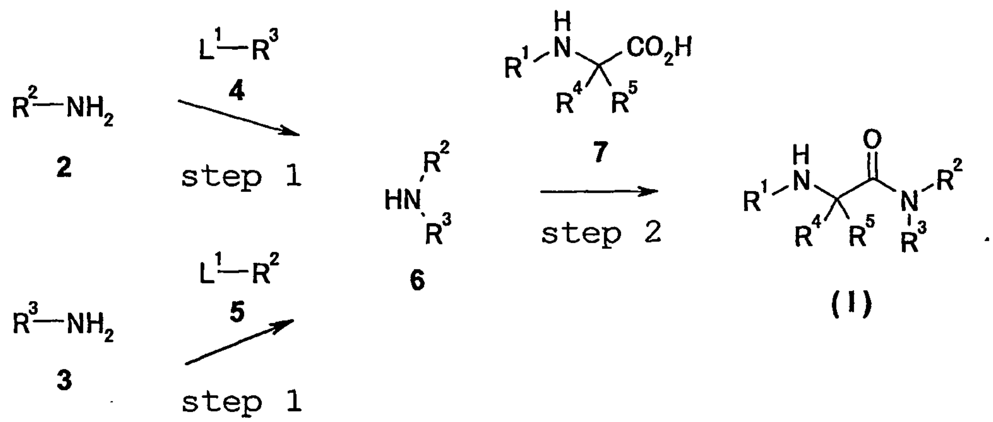
HSD-1 inhibitor, GPR40 receptor agonist, pyruvate dehydrogenase kinase (PDHK) inhibitor, microsomal triglyceride transfer protein (MTP) inhibitor, diacylglycerol acyltransferase (DGAT) inhibitor, cholesteryl ester transfer protein (CETP) inhibitor, HMG-CoA reductase inhibitor, β3 adrenaline receptor agonist, apolipoprotein-A1 (Apo-A1) inducer, lipoprotein lipase (LPL) activator, glucose-dependent insulinotropic polypeptide (GIP) receptor antagonist, leptin receptor agonist, bombesin receptor subtype 3 (BRS-3) agonist, perilipin inhibitor, acetyl-CoA carboxylase 1 (ACC1) inhibitor, acetyl-CoA carboxylase 2 (ACC2) inhibitor, melanocortin (MC) receptor agonist, neuropeptide Y5 (NPY5) receptor antagonist, adiponectin receptor agonist, protein kinase β (PKCβ) inhibitor, endothelial lipase inhibitor, angiotensin II receptor antagonist, aldose reductase inhibitor, angiotensin conversion enzyme (ACE) inhibitor, advanced glycation end products (AGE) production suppressant, glutamine/fructose-6-phosphate aminotransferase (GFAT) inhibitor, uncoupling protein (UCP) inducer/activator and the like can be mentioned.

The compound [I] of the present invention may contain various isomers, such as optical isomers, stereoisomers such as trans or cis isomers or S or R optical isomers or enantiomeric or diastereomeric forms or in mixtures thereof, geometric isomers, tautomers and the like. The present invention encompasses all of these isomers and mixtures thereof.

Now, the production methods of compound [I] of the present invention are specifically explained. It is needless to say that the present invention is not limited by these production methods. For production of the compound of the present invention, the production can be started from a part that permits easily production. When a reactive functional group is involved in each step, protection and deprotection are appropriately performed, and to promote progress of the reaction, a reagent other than the exemplified reagents can be appropriately used. In some cases, a reagent immobilized on polystyrene or silica gel may be used to

facilitate the work-up. The compound obtained in each step can be isolated and purified by conventional methods (e.g., extraction, concentration, filtration, recrystallization, column chromatography, thin layer chromatography etc.). Where desired, the compound may be used in the next step without isolation and purification.

Scheme 1



wherein L^1 is a leaving group such as halogen atom, methanesulfonyloxy, p-toluenesulfonyloxy and the like, and other symbols are as defined above.

Step 1

Compound (6) can be obtained by reacting compound (2) or compound (3) with compound (4) or compound (5) in a solvent such as N,N-dimethylformamide, tetrahydrofuran, dioxane, dichloromethane, chloroform, 1,2-dichloroethane and the like in the presence of a base, such as amines (e.g., triethylamine, diisopropylethylamine and the like) or an inorganic base (e.g., potassium carbonate, sodium hydrogen carbonate and the like), or using compound (2) or compound (3) itself as a base. In this case, a reaction additive such as sodium iodide and the like can be added to promote the reaction. The reaction is carried out at 0°C to 100°C.

Step 2

Compound [I] can be obtained from compound (6) and compound

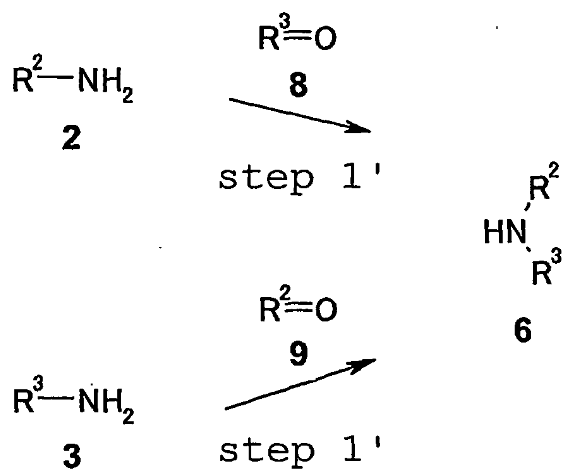
(7) using a conventional amidation reaction. A solvent such as N,N-dimethylformamide, tetrahydrofuran, dioxane, toluene, dichloromethane, chloroform, ethyl acetate and the like can be used. Examples of the amidation agent include 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, dicyclohexylcarbodiimide, O-benzotriazol-1-yl-N,N,N',N'-tetramethyluronium hexafluorophosphate, (benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate, carbonyl diimidazole, carbodiimide resin and the like. In some cases, an activator such as 1-hydroxybenzotriazole, hydroxysuccinimide, 4-dimethylaminopyridine and the like can be used. In this case, a base can be used and examples of the base include amines such as triethylamine, diisopropylethylamine, pyridine and the like, and inorganic bases such as potassium carbonate, sodium hydrogen carbonate and the like. The reaction can be carried out at -50°C to 50°C.

Compound [I] can be also obtained by treating compound (7) with a halogenating agent such as thionyl chloride, phosphorus trichloride and the like to give an acid halide, which is then condensed with compound (6). In this case, a base can be used, and examples of the base include amines such as triethylamine, diisopropylethylamine, pyridine and the like, inorganic bases such as potassium carbonate, sodium hydrogen carbonate and the like, and the like. A solvent such as tetrahydrofuran, dioxane, toluene, dichloromethane, chloroform, ethyl acetate and the like can be used. When a base is a liquid, the base itself can be used as a solvent. The reaction can be carried out at -50°C to 50°C.

In addition, compound [I] can be obtained by reacting compound (7) with chlorocarbonate, pivaloy chloride, p-toluenesulfonyl chloride and the like to give a mixed acid anhydride, which is then amidated with compound (6). In this case, a base can be used, and examples of the base include amines such as triethylamine, diisopropylethylamine, pyridine and the like, inorganic bases such as potassium carbonate, sodium hydrogen

carbonate and the like, and the like. A solvent such as tetrahydrofuran, dioxane, toluene, dichloromethane, chloroform, ethyl acetate and the like can be used. The reaction can be carried out at -50°C to 50°C.

Scheme 2

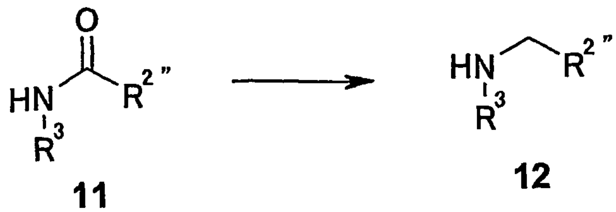


wherein each symbol is as defined above.

Step 1'

Compound (6) can be prepared by reacting compound (2) or compound (3) with compound (8) or compound (9), followed by reduction. As the reduction, for example, a method using a reducting agent such as sodium borohydride, sodium cyanoborohydride, sodium triacetoxyborohydride and the like, a hydrogenation reaction using a metal catalyst such as palladium and the like can be mentioned. Optionally, an acid such as acetic acid and the like may be added to promote the reaction. A solvent that does not affect the reaction, such as ethanol, methanol, tetrahydrofuran, dioxane, water, chloroform and the like can be mentioned. The reaction can be carried out at -20°C to 100°C.

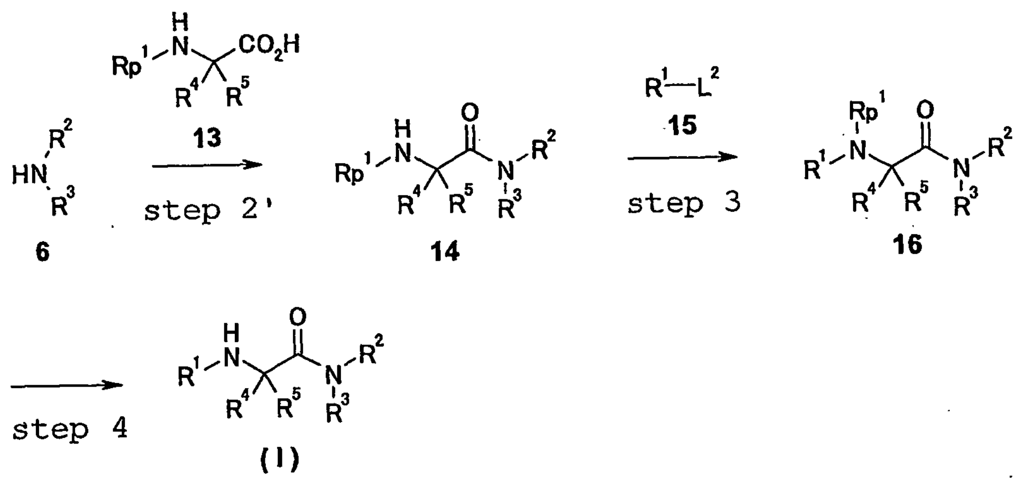
Scheme 3



wherein $R^{2''}$ is hydrogen atom or C_{1-5} alkyl, and R^3 is as defined above.

Compound (12), which is a compound (6) wherein R^2 is C_{1-6} alkyl, can be obtained by reduction of compound (11). As the reducing agent, lithium aluminum hydride, sodium borohydride, borane and the like can be mentioned. A solvent such as diethyl ether, dioxane, tetrahydrofuran and the like can be used. The reaction can be carried out at 0°C to 100°C.

Scheme 4



wherein Rp^1 is an amino protecting group such as tert-butoxycarbonyl, benzyloxycarbonyl and the like, L^2 is a leaving group such as halogen atom, methanesulfonyloxy, p-toluenesulfonyloxy and the like and other symbols are as defined above.

Step 2'

Compound (14) can be obtained by reacting under the same conditions as described in Step 2 and using compound (13) instead of compound (7) shown in Step 2 of the aforementioned Scheme 1.

Step 3

Compound (16) can be obtained by reacting compound (14) and compound (15) under the same conditions as described in Step 1 of the aforementioned Scheme 1.

Step 4

In this step, compound [I] is introduced by removing an amino protecting group Rp^1, and a conventional deprotection method can be used. For example, when Rp^1 is a group deprotected by an acid, such as tert-butoxycarbonyl, trityl, o-nitrobenzenesulfenyl and the like, the deprotection can be performed using an acid such as hydrochloric acid, hydrobromic acid, sulfuric acid, trifluoroacetic acid, formic acid, p-toluenesulfonic acid, methanesulfonic acid and the like. A solvent such as ethanol, methanol, tetrahydrofuran, ethyl acetate, acetic acid, N,N-dimethylformamide, dichloromethane, chloroform, 1,2-dichloroethane and the like can be mentioned. In this case, the deprotection can be performed using an acid appropriately diluted with or dissolved in an organic solvent or water. The reaction can be carried out at -50°C to 50°C.

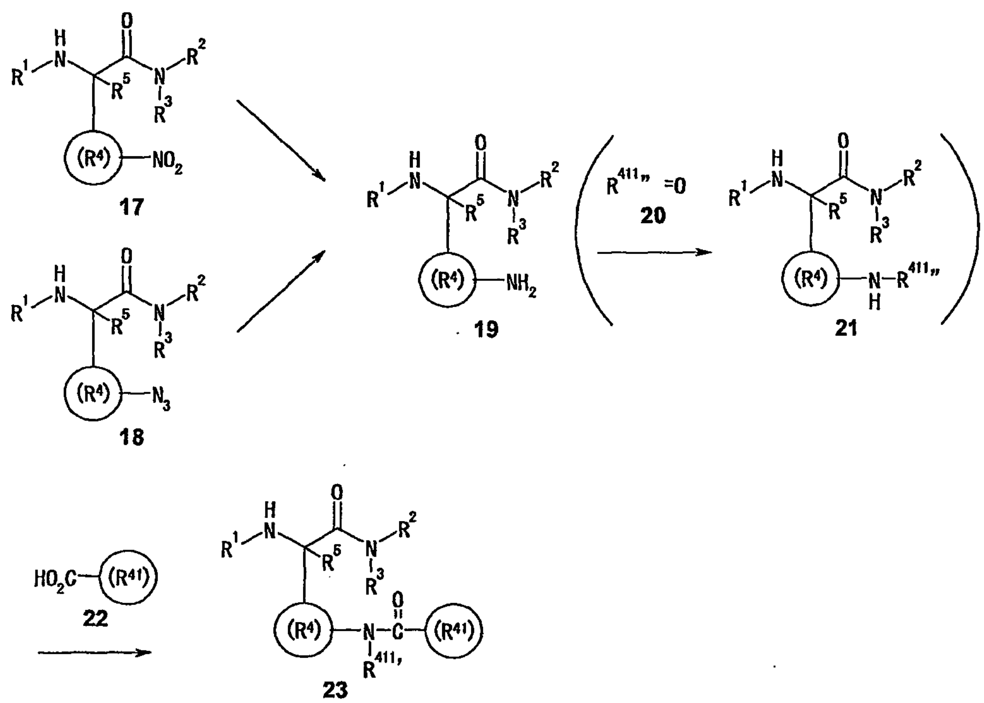
When, Rp^1 is a group deprotected by a hydrogenation reaction using benzyloxycarbonyl and the like, it can be deprotected by a hydrogenation reaction using metal catalyst such as palladium and the like. A solvent that does not affect the reaction, such as ethanol, methanol, tetrahydrofuran, ethyl acetate, acetic acid and the like can be used. The reaction can be also carried out using ammonium formate, cyclohexene and the like, besides a method using a hydrogen gas under atomospheric pressure or under pressure condition. The reaction can be carried out at 0°C to 100°C.

When, Rp^1 is a protecting group deprotected by a base such as fluorenylmethoxycarbonyl and the like, it can be deprotected using a base such as diethylamine, piperidine, ammonia, sodium hydroxide, potassium carbonate and the like. These bases can be used as they are, or after dilution with, dissolution in or suspending in a solvent. A solvent such as water, ethanol,

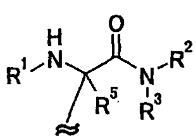
methanol, tetrahydrofuran, ethyl acetate, N,N-dimethylformamide, dichloromethane, chloroform, 1,2-dichloroethane and the like can be used. The reaction can be carried out at 0°C to 100°C.

When, Rp^1 is a group deprotected by a metal catalyst such as allyloxycarbonyl and the like, it can be deprotected using tetrakis(triphenylphosphine)palladium and the like as a catalyst or reagent. In this case, a solvent that dose not affect the reaction (e.g., dichloromethane, chloroform, tetrahydrofuran and the like) is used. The reaction can be carried out at 0°C to 100°C.

Scheme 5



wherein

(R^4) is, of the parts represented by R^4, a part that is bonded to  and also adjacent to $-CONR^{411}-$, $-NR^{411}CO-$, $-CSNR^{411}-$, $-NR^{411}CS-$, $-NR^{411}SO_2-$, $-SO_2NR^{411}-$, $-NR^{411}CO_2-$, $-OCONR^{411}-$, $-NR^{411}CONR^{412}-$ or $-NR^{411}CSNR^{412}-$, (R^{41}) is, of the parts represented by R^4, a part

on the end via $-CONR^{411}-$, $-NR^{411}CO-$, $-CSNR^{411}-$, $-NR^{411}CS-$, $-NR^{411}SO_2-$, $-SO_2NR^{411}-$, $-NR^{411}CO_2-$, $-OCONR^{411}-$, $-NR^{411}CONR^{412}-$ or $-NR^{411}CSNR^{412}-$, $R^{411'}$ is hydrogen atom or optionally substituted C_{1-6}alkyl, $R^{411''}$ is optionally substituted C_{1-6}alkyl, and other symbols are as defined above.

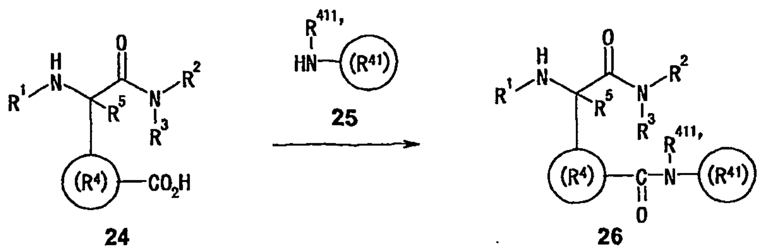
Compound (19) can be obtained by reduction of compound (17) or (18). In the case of compound (17), compound (19) can be obtained by a method comprising hydrogenation using a catalyst such as palladium on carbon, palladium black, palladium hydroxide on carbon and the like, a method comprising combining a metal, such as iron, zinc, tin chloride and the like, and an acid, such as hydrochloric acid, acetic acid, ammonium chloride and the like, a method using sodium hydrosulfite, and the like. As the solvent, a solvent that does not influence the reaction, such as methanol, ethanol, tetrahydrofuran, water, ethyl acetate and the like, can be used. The reaction can be carried out at 0°C to 100°C.

In the case of compound (18), compound (19) can be obtained by a method comprising hydrogenation using a catalyst such as palladium on carbon, palladium black, palladium hydroxide on carbon and the like, a method using a reducing agent such as sodium borohydride, lithium borohydride, sodium cyanoborohydride, lithium aluminum hydride, diisobutylaluminum hydride and the like, a method using triphenylphosphine as a reducing agent, and the like. A solvent that does not affect the reaction, such as methanol, ethanol, tetrahydrofuran, water, ethyl acetate and the like can be used, The reaction can be carried out at 0°C to 100°C.

When a compound wherein R^{411} is optionally substituted C_{1-6}alkyl is desired, compound (21) can be obtained by the method shown in the aforementioned Scheme 2, Step 1' and using compound (19) and compound (20).

Compound (23) can be obtained by the method shown in the aforementioned Scheme 1, Step 2 and using compound (19) or compound (21) and compound (22).

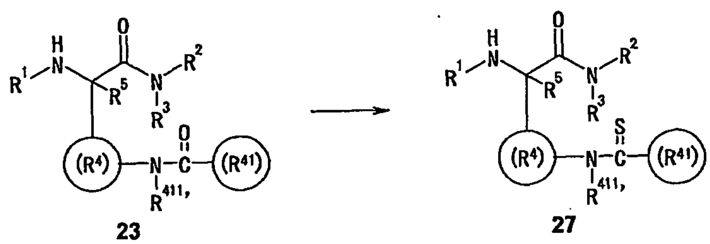
Scheme 6



wherein each symbol is as defined above.

Compound (26) can be obtained by the method shown in the aforementioned Scheme 1, Step 2, and using compound (24) and compound (25).

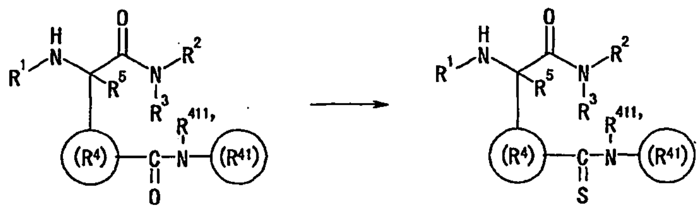
Scheme 7



wherein each symbol is as defined above.

Compound (27) can be obtained by reacting a sulfidizing agent such as Lawesson's reagent, phosphorus pentasulfide and the like with compound (23). In this case, a solvent that does not affect the reaction such as methanol, tetrahydrofuran, dioxane and the like can be used as a solvent. The reaction can be carried out at 0°C to 100°C. The moiety easily affected by this reaction can be appropriately protected in advance. In addition, the order of production may be changed as appropriate.

Scheme 8

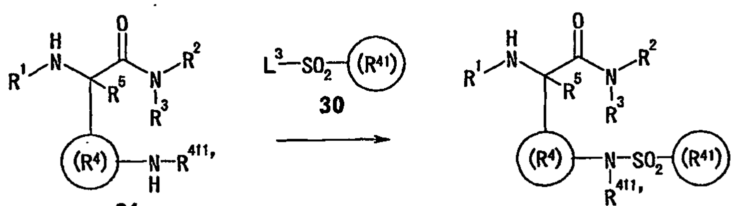


26 28

wherein each symbol is as defined above.

Compound (28) can be obtained by the method shown in the aforementioned Scheme 7 and using compound (26).

Scheme 9

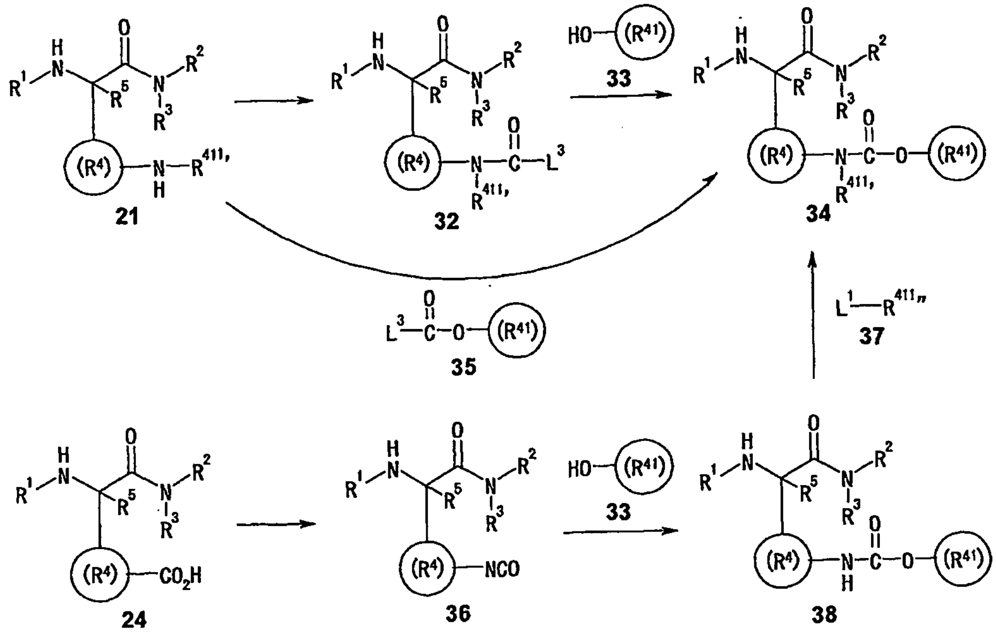


21 30 31

wherein L^3 is a leaving group such as halogen atom and the like and other symbols are as defined above.

Compound (31) can be obtained by reacting compound (21) with compound (30). In this case, a base can be used, and examples of the base include amines such as triethylamine, diisopropylethylamine, pyridine and the like, inorganic bases such as potassium carbonate, sodium hydrogen carbonate and the like, and the like. A solvent such as tetrahydrofuran, dioxane, toluene, dichloromethane, chloroform, ethyl acetate and the like can be used. When the base is a liquid, the base itself can be used as a solvent. The reaction can be carried out at -50°C to 50°C.

Scheme 10



wherein each symbol is as defined above.

Compound (34) can be obtained by reacting carbamoyl halide (32) obtained from compound (21), or isocyanate (36) obtained from compound (24) with compound (33).

In the case of compound (21), phosgene, triphosgene, 1,1'-carbonyldiimidazole and the like are reacted to give compound (32), which is then reacted with compound (33) to give compound (34). In this case, a base can be used, and examples of the base include amines such as triethylamine, diisopropylethylamine, pyridine and the like, inorganic bases such as potassium carbonate, sodium hydrogen carbonate and the like, and the like. A solvent such as tetrahydrofuran, dioxane, toluene, dichloromethane, chloroform, ethyl acetate and the like can be used. The reaction can be carried out at -50°C to 50°C.

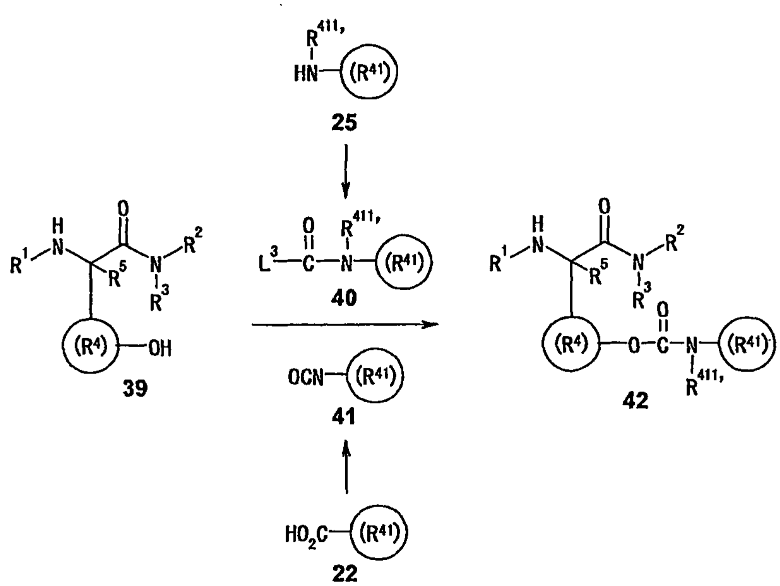
Compound (34) can be also obtained by the method shown in the aforementioned Scheme 1, Step 1, and using compound (21) and compound (35).

In the case of compound (24), compound (38) can be obtained by reacting compound (33) with compound (36) obtained by reacting lithium azide or sodium azide with an acid halide obtained by

treating a halogenation agent such as thionyl chloride, phosphorus trichloride and the like or a mixed acid anhydride obtained by reacting with chlorocarbonate, pivaloyl chloride, p-toluenesulfonyl chloride and the like, or by heating acid azide obtained by reacting diphenylphosphoryl azide with compound (24). In this case, a base can be used, and examples of the base include amines such as triethylamine, diisopropylethylamine, pyridine and the like, inorganic bases such as potassium carbonate, sodium hydrogen carbonate and the like, and the like can be mentioned. A solvent such as tetrahydrofuran, dioxane, toluene, dichloromethane, chloroform, ethyl acetate and the like can be used. The reaction can be carried out at 0°C to 100°C.

When a compound wherein R^{411} is optionally substituted C_{1-6}alkyl is desired, compound (34) can be obtained by the method shown in the aforementioned Scheme 1, Step 1, and using compound (38) and compound (37).

Scheme 11



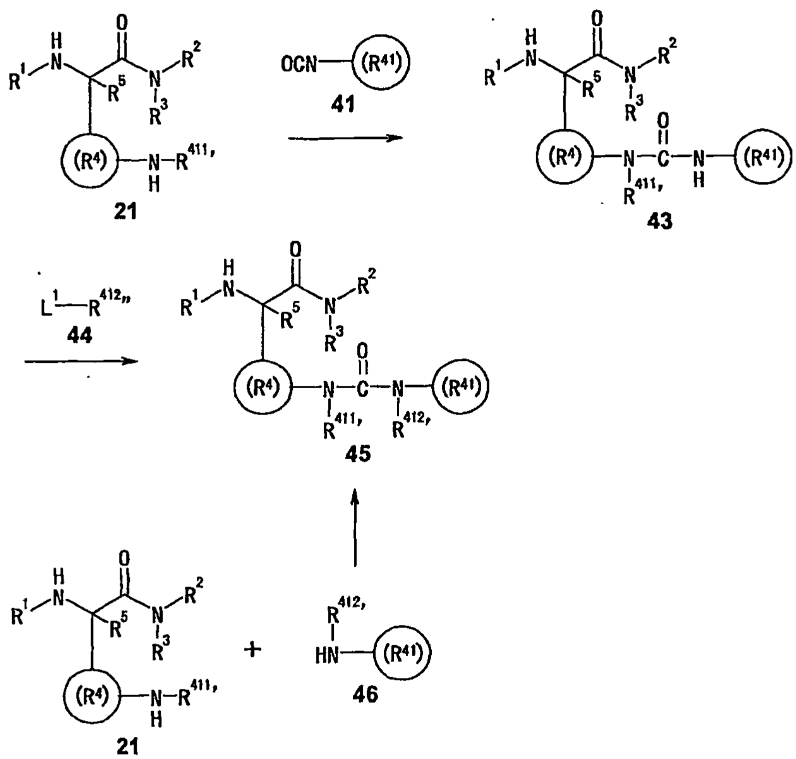
wherein each symbol is as defined above.

Compound (42) can be obtained by the method shown in the aforementioned Scheme 10, and using compound (39) and compound (40) or compound (41).

Compound (40) can be obtained from compound (25) by the same

method to obtain compound (32) as shown in the aforementioned Scheme 10. In addition, Compound (41) can be obtained from compound (22) by the same method to obtain compound (36) as shown in the aforementioned Scheme 10.

Scheme 12



wehrien $R^{412\prime}$ is hydrogen atom or optionally substituted C_{1-6}alkyl, $R^{412\prime\prime}$ is optionally substituted C_{1-6}alkyl and other symbols are as defined above.

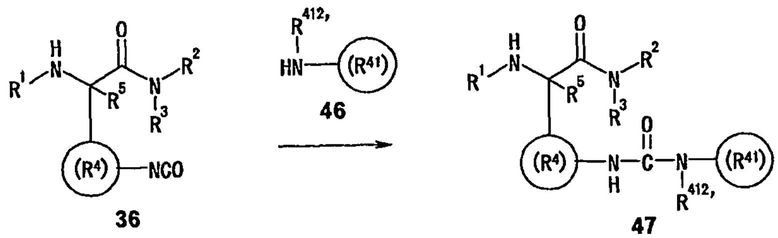
Compound (43) can be obtained by the same method as shown in the aforementioned Scheme 10 and using compound (41) to compound (21).

When a compound wherein R^{412} is optionally substituted C_{1-6}alkyl is desired, compound (45) can be obtained by reacting compound (43) with compound (44) in the presence of a base. A base such as n-butyl lithium, lithium diisopropylamide, potassium hexamethyldisilazide, sodium hydride and the like can be used. In addition, sodium iodide and the like may be added to accerelate the reaction. A solvent that does not affect the reaction, such

as tetrahydrofuran, dioxane, diethyl ether, toluene and the like, can be used. The reaction can be carried out at -100°C to 100°C.

Compound (45) can be also obtained by a method comprising reacting compound (21) and compound (46) with phosgene.

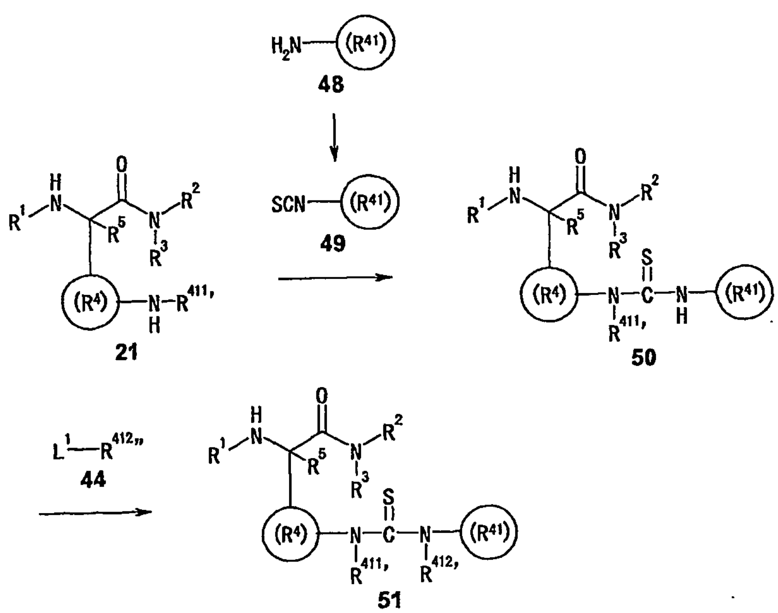
Scheme 13



wherein each symbol is as defined above.

Of compounds (45), when compound (47) wherein R^{411} is hydrogen is desired, it can be obtained by the same method to obtain compound (38) as shown in the aforementioned Scheme 10 and using compound (36) and compound (46).

Scheme 14

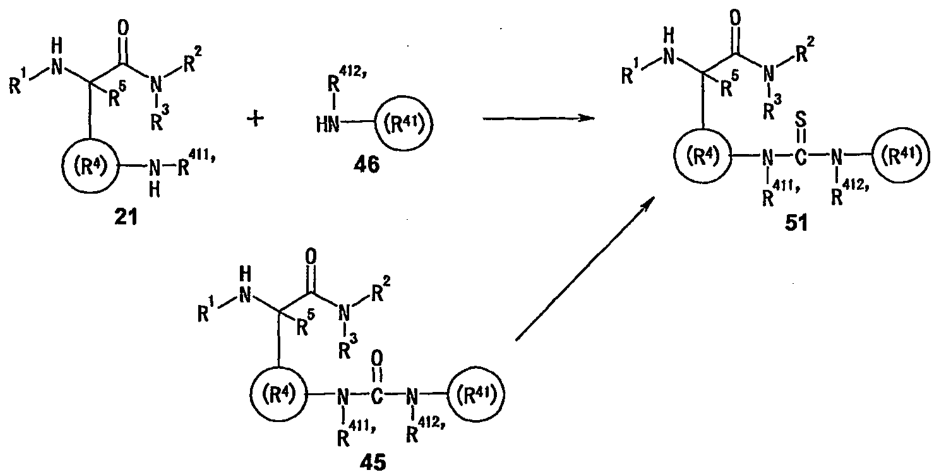


wherein each symbol is as defined above.

Compound (50) can be obtained by reacting compound (21) with compound (49). Compound (49) can be obtained by a method using carbon disulfide to compound (48).

When a compound wherein R^{412} is optionally substituted C_{1-6}alkyl is desired, compound (51) can be also obtained by the same method to obtain compound (45) as shown in the aforementioned Scheme 12 and using compound (50) and compound (44).

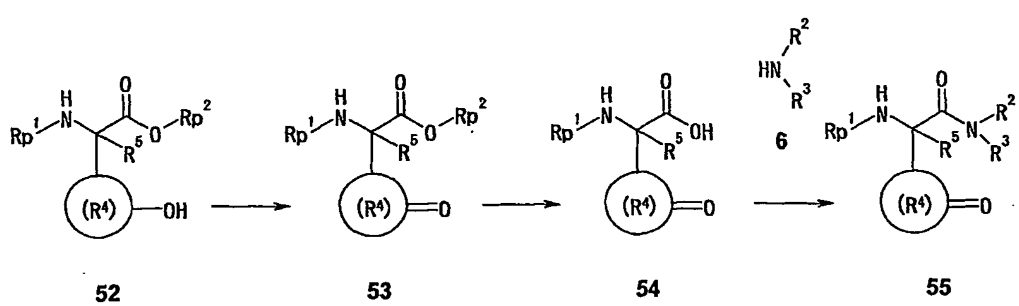
Scheme 15



wherein each symbol is as defined above.

Compound (51) can be obtained by reacting compound (21) and compound (46) with thiophosgene, or from compound (45) in the same manner as in Scheme 7.

Scheme 16



wherein Rp^2 is a carboxyl protecting group such as methyl, benzyl, tert-butyl and the like, and other symbols are as defined above.

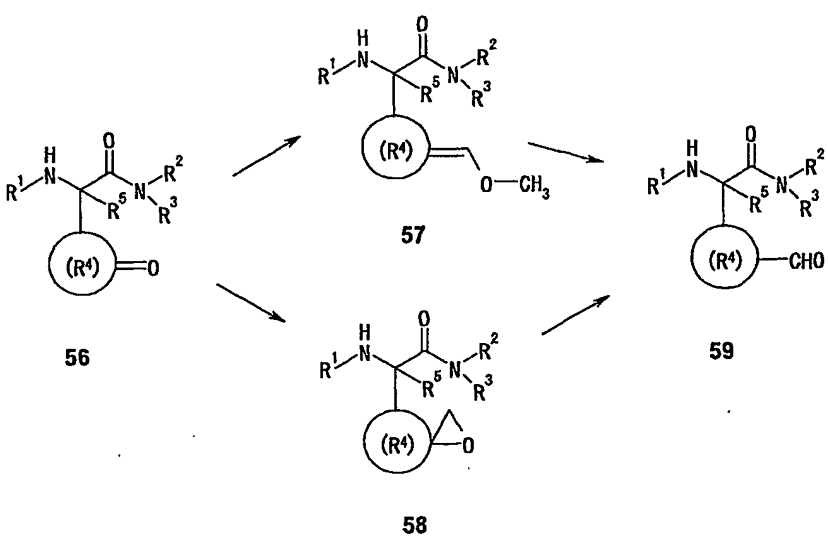
Compound (53) can be obtained by oxidation of compound (52). As an oxidation method, a conventional method for oxidizing alcohol such as a method using dimethyl sulfoxide and oxalyl chloride, a method using dimethyl sulfoxide and a sulfur trioxide-pyridine complex, a method using Dess-Martin reagent, a method using a Jones reagent and the like can be used. When dimethyl

sulfoxide is used, it can be used as a solvent. Alternatively, a solvent that dose not affect the reaction such as dichloromethane, chloroform, acetonitrile, water, tert-butanol and the like can be used. The reaction can be carried out at -78°C to 50°C.

Compound (54) can be obtained by removing the carboxyl protecting group Rp^2 of compound (53). As the deprotection method, a conventional deprotection method can be used as long as the amino protecting group Rp^1 is not deprotected. For example, when Rp^1 is a tert-butoxycarbonyl and Rp^2 is a protecting group such as methyl, benzyl and the like, which is deprotected by a base, deprotection can be performed using a base such as ammonia, sodium hydroxide, potassium carbonate and the like. These bases can be used as they are, or after dilution, dissolution or suspendeding in a solvent. In this case, as the solvent, water, ethanol, methanol, tetrahydrofuran, N,N-dimethylformamide, dichloromethane, chloroform, 1,2-dichloroethane and the like can be used. The reaction can be carried out at 0°C to 100°C.

Compound (55) can be obtained under the similar conditions as the method shown in the aforementioned Scheme 1, Step 2 and using compound (54) and compound (6).

Scheme 17



each symbol is as defined above.

Compound (59) can be obtained by hydrolyzing compound (57).

or isomerizing compound (58).

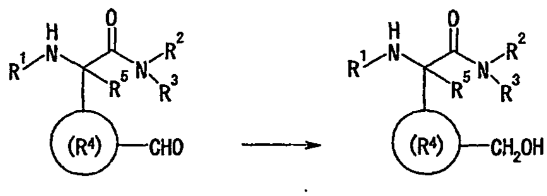
Compound (57) can be obtained by reacting compound (56) with methoxymethyl triphenylphosphonium chloride, dimethyl (1-diazo-2-oxopropyl)phosphonate and the like in the presence of a base. A base such as sodium dimsyl, n-butyl lithium, 1,8-diazabicyclo[5.4.0]undec-7-ene, sodium hydride, potassium carbonate, sodium hydroxide and the like can be used. A solvent that dose not affect the reaction such as tetrahydrofuran, dioxane, toluene, methanol, dimethyl sulfoxide, N,N-dimethylformamide and the like can be used. The reaction can be carried out at 0°C to 100°C.

Compound (59) can be obtained by reacting compound (57) with trichloroacetic acid, trifluoroacetic acid, trimethylsilyl iodide and the like. As the solvent, a solvent that is not involved in the reaction such as tetrahydrofuran, dioxane, acetonitrile, dichloromethane, chloroform and the like can be used. The reaction can be carried out at 0°C to 100°C.

Compound (58) can be obtained by reacting compound (56) with trimethylsulfonium chloride, trimethylsulfoxonium chloride and the like in the presence of a base. A base such as sodium dimsyl, n-butyl lithium, 1,8-diazabicyclo[5.4.0]undec-7-ene, sodium hydride and the like can be used, and as the solvent, a solvent that dose not affect the reaction such as tetrahydrofuran, dioxane, toluene, dimethyl sulfoxide, N,N-dimethylformamide and the like can be used. The reaction can be carried out at -78°C to -100°C.

Compound (59) can be obtained by reacting compound (58) with a Lewis acid such as boron trifluoride, aluminum chloride, magnesium bromide, titanium tetrachloride and the like. As the solvent, a solvent that is not involved in the reaction such as diethyl ether, diisopropyl ether, tetrahydrofuran, dimethoxyethane, dioxane and the like can be used. The reaction can be carried out at 0°C to 100°C.

Scheme 18

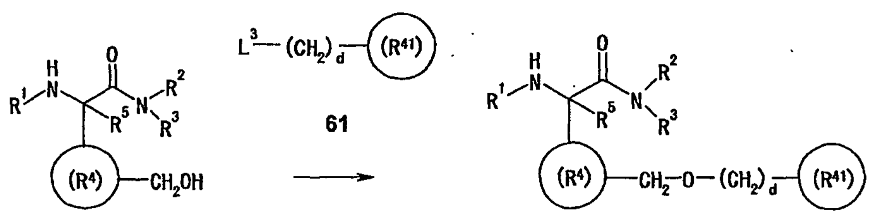


59 60

wherein each symbol is as defined above.

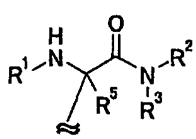
Compound (60) can be obtained by reduction of compound (59). A reducing agent such as sodium borohydride, lithium borohydride, lithium aluminum hydride, diisopropylaluminum hydride and the like can be used. A solvent that dose not affect the reaction such as methanol, tetrahydrofuran, diethyl ether, toluene, benzene and the like can be used. The reaction can be carried out at 0°C to 100°C.

Scheme 19



61

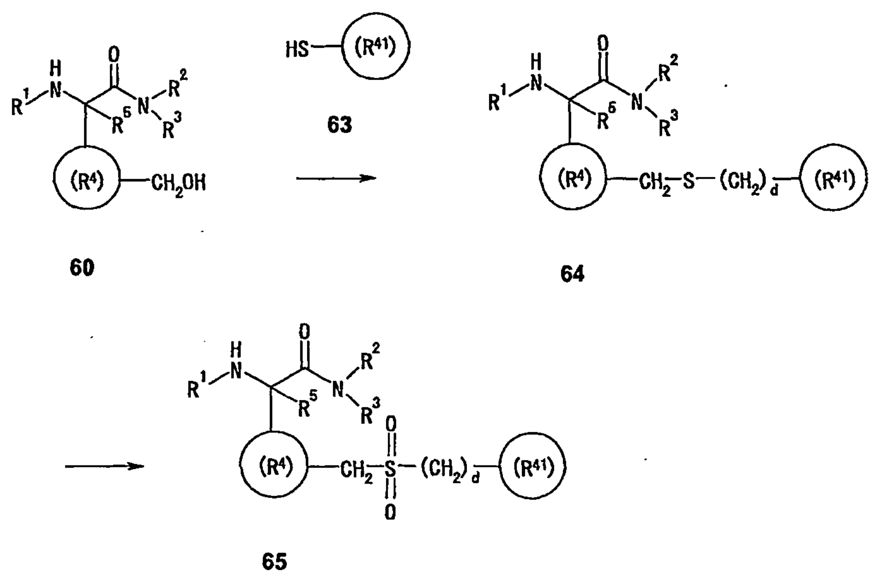
60 62

wherein (R^4) is, of the parts represented by R^4, a part that is bonded to  and also adjacent to $-CH_2-O-(CH_2)_d-$, $-CH_2-S-(CH_2)_d-$ or $-CH_2-SO_2-(CH_2)_d-$ and (R^{41}) is, of the parts represented by R^4, a part on the end via $-CH_2-O-(CH_2)_d-$, $-CH_2-S-(CH_2)_d-$ or $-CH_2-SO_2-(CH_2)_d-$, and other symbols are as defined above.

Compound (62) can be obtained by reacting compound (60) with compound (61). In this case, the reaction can be carried out in the presence of one or both of a silver compound such as silver oxide, silver trifluoromethanesulfonate and the like, and a base such as sodium hydride, potassium tert-butoxide, 2,6-lutidine,

2,6-di-tert-butyl-4-methylpyridine and the like. A solvent that dose not affect the reaction such as dichloromethane, chloroform, tetrahydrofuran, dioxane, dimethoxyethane, toluene, benzene, N,N-dimethylformamide and the like can be used. The reaction can be carried out at 0°C to 100°C.

Scheme 20

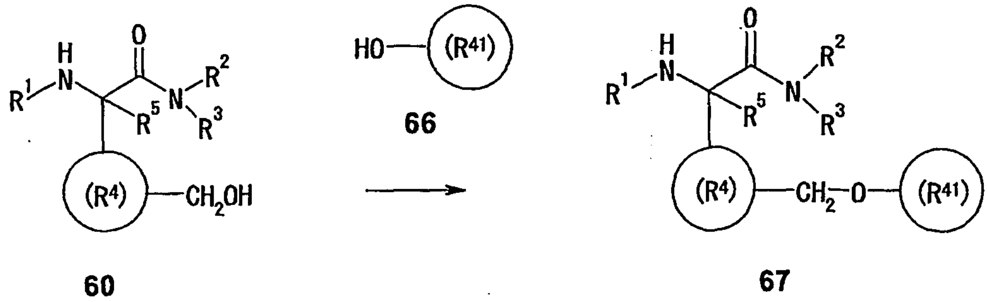


wherein each symbol is as defined above.

Compound (64) can be obtained by Mitsunobu reaction using compound (60) and compound (63), triphenylphosphine and diisopropyl azodicarboxylate or diethyl azodicarboxylate. A solvent that dose not affect the reaction such as dichloromethane, chloroform, tetrahydrofuran, dioxane, dimethoxyethane and the like can be used. The reaction can be carried out at 0°C to 100°C.

Compound (65) can be obtained by oxidation of compound (64). As the oxidant, peroxy acids such as m-chloroperoxybenzoic acid, peroxyacetic acid and the like or potassium permanganate can be used. A solvent that dose not affect the reaction such as dichloromethane, chloroform, tetrahydrofuran, dioxane, dimethoxyethane and the like can be used. The reaction can be carried out at 0°C to 100°C.

Scheme 21



wherein each symbol is as defined above.

Compound (67) means compound (62) wherein d is 0. In this case, the following method may be used.

Compound (67) can be obtained by subjecting compound (60) to Mitsunobu reaction using compound (66), triphenylphosphine and diisopropyl azodicarboxylate or diethyl azodicarboxylate. A solvent that dose not affect the reaction such as dichloromethane, chloroform, tetrahydrofuran, dioxane, dimethoxyethane, and the like can be used. The reaction can be carried out at 0°C to 100°C.

In each of the above-mentioned production methods, a compound wherein suitable substituent R^1 has been introduced can be produced by producing a compound wherein R^1 is an amino protecting group Rp^1, and reacting the obtained amino-protected form under the same conditions as for the method shown in Step 3 and Step 4 of the aforementioned Scheme 4. In addition, a compound wherein R^1 is hydrogen atom can be obtained by removing the amino protecting group Rp^1 from the deprotected amino form under the same conditions as for the method shown in the aforementioned Scheme 4, Step 4.

The thus-obtained compound [I] of the present invention has a superior DPP-IV inhibitory activity. When the compound of the present invention is used as a therapeutic drug for type II diabetes, especially type II diabetes, as well as hyperglycemia, hypoglycemia, Syndrome X, diabetic complications, hyperinsulinemia, obesity, atherosclerosis and related diseases thereof, anxiety, eating disorders, neurodegenerative diseases, as well as various immunomodulatory diseases including psoriasis, multiple sclerosis, rheumatoid arthritis, and chronic inflammatory bowel disease, for

organ transplantation, it is generally administered systemically, or topical, orally or parenterally.

While the dose varies depending on the age, body weight, symptoms, treatment effect, administration method, treatment time and the like, it is generally from 0.01 mg to 10 g, preferably 1 mg to 1 g, for an adult per day, which is orally or parenterally administered once a day to several portions a day.

When the compound of the present invention is processed to give a solid composition for oral administration, a dosage form such as tablet, pill, powder, granule and the like can be employed. In such a solid composition, one or more active substance is admixed with at least one inactive diluent, dispersant, adsorbent and the like, such as lactose, mannitol, glucose, hydroxypropyl cellulose, microcrystalline cellulose, starch, polyvinyl pyrrolidone, magnesium aluminometasilicate, slicon dioxide powder and the like. The composition may be mixed with an additive other than a diluent according to conventional methods.

When a tablet or a pill is to be prepared, it may be coated with a film made from an enteric or gastrosoluble substance as necessary such as sucrose, gelatin, hydroxypropyl cellulose, hydroxymethylcellulose phthalate and the like, or coated with two or more layers. In addition, a capsule made from a substance such as gelatin or ethyl cellulose can be produced.

When a liquid composition for oral administration is desired, a dosage form such as a pharmaceutically acceptable emulsifier, solubilizer, suspension, syrup, elixir and the like can be employed. As the diluent to be used, for example, purified water, ethanol, vegetable oil, emulsifier and the like can be mentioned. The composition may further contain an auxiliary agent other than diluent, such as humectant, suspension, sweetening agent, flavor, aromatic, preservative and the like.

When an injection for parenteral administration is to be prepared, a sterile aqueous or non-aqueous solution, solubilizer, suspension or emulsifier can be used. As an aqueous solution,

solubilizer or suspension, for example, distillated water for injection, physiological saline, cyclodextrin and derivative thereof, organic amines such as triethanolamine, diethanolamine, monoethanolamine, triethylamine and the like, inorganic alkaline solution and the like can be mentioned.

When a water-soluble solution is desired, for example, propylene glycol, polyethylene glycol, vegetable oil such as olive oil, alcohols such as ethanol and the like may be also used. As a solubilizer, for example, surfactants (for forming mixed micelle) such as polyoxyethylene hydrogenated castor oil, sucrose esters, fatty acids and the like, or lecithin or hydrogenated lecithin (for forming liposome) and the like can be used. In addition, an emulsion preparation comprising a non-water-soluble solubilizer such as vegetable oil and the like, and lecithin, polyoxyethylene hydrogenated castor oil, polyoxyethylene polyoxypropyleneglycol and the like can be also prepared.

As other composition for parenteral administration, a coating agent such as external liquid and ointment, suppository, pessary and the like, which contains one or more active substances and which can be prepared by a method known *per se* can be produced.

Compound [I] can be used alone for the treatment of diabetes and may be used in combination with other pharmaceutical components including other therapeutic drugs for diabetes, therapeutic drugs for diabetic complications, therapeutic drugs for hyperlipidemia or anti-obesity drugs. In this case, these compounds are preferably administered as oral preparations, and where necessary, they may be administered in the form of a suppository and the like.

As used herein, the mode of the combined use of compound [I] with the other pharmaceutical components is not particularly limited. For example, it includes both the administration of a pharmaceutical composition containing the compound [I] and the other pharmaceutical components, and the simultaneous or staggered administration of respective preparations produced separately

without mixing.

While the dose of the other pharmaceutical components varies depending on the age, body weight, symptoms, treatment effect, administration method, treatment time and the like, it is generally from 0.01 mg to 10 g, preferably 1 mg to 1 g, for an adult per day, which is orally or parenterally administered once a day to several portions a day.

In this case, as a therapeutic drug for diabetes, a therapeutic drug for diabetic complications, a therapeutic drug for hyperlipidemia and an anti-obesity drug, that can be combined, for example, insulin preparations (injections), low-molecular weight insulin preparations (oral agents), sulfonylurea receptor agonists (SU drugs), short acting insulin secretagogues (e.g., nateglide), α-glucosidase inhibitors, insulin sensitizers, PPARα receptor agonists, PPARγ receptor agonists/antagonists, PPARδ receptor agonists, tGLP-1 receptor agonists, glucagon receptor antagonists, glucocorticoid receptor antagonists, biguanides, SGLUT inhibitors, fructose-1,6-bisphosphatases (FBPase) inhibitors, glycogen synthase kinase 3 (GSK-3) inhibitors, phosphoenolpyruvate carboxykinase (PEPCK) inhibitors, protein tyrosine phosphatase 1B (PTPase 1B) inhibitors, SH2 domain-containing inositol phosphatase (SHIP2) inhibitors, AMP-activated protein kinase (AMPK) activators, glycogen phosphorylase (GP) inhibitors, glucokinase activators, 11β-HSD-1 inhibitors, GPR40 receptor agonists, pyruvate dehydrogenase kinase (PDHK) inhibitors, microsomal triglyceride transfer protein (MTP) inhibitors, diacylglycerol acyltransferase (DGAT) inhibitors, cholesteryl ester transfer protein (CETP) inhibitors, HMG-CoA reductase inhibitors, β3 adrenaline receptor agonists, apolipoprotein-A1 (Apo-A1) inducers, lipoprotein lipase (LPL) activators, glucose-dependent insulinotropic polypeptide (GIP) receptor antagonists, leptin receptor agonists, bombesin receptor subtype 33 (BRS-3) agonists, perilipin inhibitors, acetyl-CoA carboxylase 1 (ACC1) inhibitors, acetyl-CoA carboxylase 2 (ACC2) inhibitors, melanocortin (MC) receptor agonists,

neuropeptide Y5 (NPY5) receptor antagonists, adiponectin receptor agonists, protein kinaseβ (PKCβ) inhibitors, endothelial lipase inhibitors, angiotensin II receptor antagonists, aldose reductase inhibitors, angiotensin conversion enzyme (ACE) inhibitors, advanced glycation end products (AGE) inhibitors, glutamine/fructose-6-phosphate aminotransferase (GFAT) inhibitors, uncoupling protein (UCP) inducers/activators and the like can be mentioned.

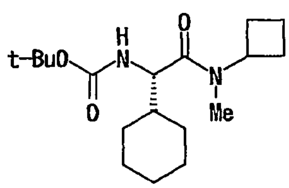
Examples

The compound [I] and the production method therof of the present invention are explained in detail by referring to the following Examples, which are not to be construed as limitative.

Example 1

Step 1

(2S)-N-Cyclobutyl-N-methyl-2-(tert-butoxycarbonylamino)-2-cyclohexylacetamide



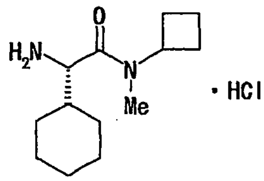
N-Methylcyclobutylamine hydrochloride (159 mg) synthesized by the method described in Journal of Medicinal Chemistry, 1994, 37, 3482 was dissolved in N,N-dimethylformamide (4 ml), and L-tert-butoxycarbonylcyclohexylglycine hydrate (159 mg), (benzotriazole-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate (676 mg) and diisopropylethylamine (0.453 ml) were added. The mixture was stirred overnight at room temperature. The mixture was poured into water and extracted with ethyl acetate. The organic layer was washed successively with saturated aqueous sodium hydrogen carbonate solution, 5% aqueous potassium hydrogen sulfate solution and saturated brine, and dried over sodium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure and the residue was purified by silica gel chromatography (hexane:ethyl acetate=3:1) to give

the title compound.

^{1}H-NMR(δppm,$CDCl_3$) 1.13-1.37(5H,m), 1.42(9H,s), 1.59-1.71(9H,m), 2.10-2.29 (4H,m), 4.39-4.55(1H,m), 4.80-4.90(0.4H,m), 5.25-5.33(0.6H,m).

Step 2

(2S)-N-Cyclobutyl-N-methyl-2-amino-2-cyclohexylacetamide hydrochloride



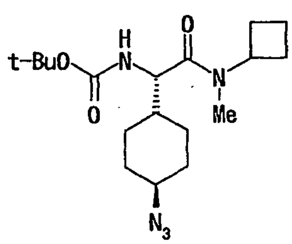
(2S)-N-Cyclobutyl-N-methyl-2-(tert-butoxycarbonylamino)-2-cyclohexylacetamide (280 mg) was suspended in ethyl acetate (1 ml), and a solution of 4N-hydrogen chloride in ethyl acetate was added. The mixture was stirred for 5 hr at room temperature. The reaction mixture was concentrated under reduced pressure, ethyl acetate was added to the residue and the mixture was stirred. The precipitated solid was collected by filteration, washed with ethyl acetate and dried under reduced pressure to give the title compound.

^{1}H-NMR(δppm,DMSO-d_6) 1.03-1.18(5H,m), 1.59-1.73(8H,m), 1.99-2.28(4H,m), 2.88(1.7H,s), 2.98(1.3H,s), 4.10(0.4H,d,J=5.4Hz), 4.26(0.6H,d,J=5.4Hz), 4.42-4.58(0.6H,m), 4.69-4.80(0.4H,m), 8.12(3H,brs).

Example 29

Step 1

(S)-[(trans-4-Azidocyclohexyl)-(N-cyclobutyl-N-methylcarbamoyl)methyl]carbamic acid tert-butyl ester



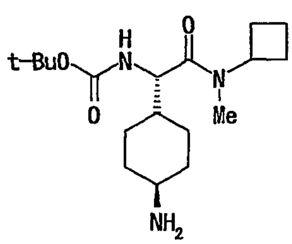
(S)-N-tert-Butoxycarbonyl-(trans-4-azidocyclohexyl)glycine

(2.72 g) synthesized in accordance with the method described in WO02/076450, N-methylcyclobutylamine hydrochloride (1.1 g) synthesized in accordance with the method described in Journal of Medicinal Chemistry, 1994, 37, 3482, and triethylamine (3.17 ml) were dissolved in N,N-dimethylformamide (25 ml), and (benzotriazole-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate (5.2 g) was added. The mixture was stirred overnight at room temperature. The reaction mixture was poured into water and extracted with ethyl acetate. The organic layer was washed successively with saturated aqueous sodium hydrogen carbonate solution and saturated brine, and dried over sodium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure and the residue was purified by silica gel chromatography (ethyl acetate:hexane=2:5-1:2) to give the title compound (2.84 g).

^{1}H-NMR(δppm,$CDCl_3$) 1.06-1.37(4H,m), 1.42(9H,s), 1.45-1.80(5H,m), 1.97-2.34(6H,m), 2.92(1.8H,s), 2.99(1.2H,s), 3.13-3.24(1H,m), 4.36-4.48(1H,m), 4.51-4.58(0.6H,m), 4.78-4.89(0.4H,m), 5.26-5.37(1H,m).

Step 2

(S)-[(trans-4-Aminocyclohexyl)-(N-cyclobutyl-N-methylcarbamoyl)methyl]carbamic acid tert-butyl ester



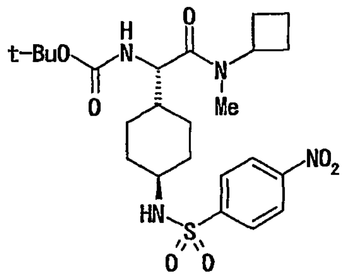
(S)-[(trans-4-Azidocyclohexyl)-(N-cyclobutyl-N-methylcarbamoyl)methyl]carbamic acid tert-butyl ester (2.78 g) obtained in Step 1 was dissolved in tetrahydrofuran (55ml)-water (5.5ml), and triphenylphosphine (2.19g) was added. The mixture was stirred for 17 hrs at room temperature. The reaction mixture was concentrated under reduced pressure and the residue was purified by silica gel chromatography (chloroform:methanol=10:1-

chloroform:methanol:28% aqueous ammonia=10:1:0.1) to give the title compound.

^{1}H-NMR(δppm, $CDCl_3$) 0.92-1.21(4H,m), 1.42(9H,s), 1.31-1.58(3H,m), 1.58-1.77(4H,m), 1.80-1.92(2H,m), 2.00-2.32(4H,m), 2.51-2.63(1H,m), 2.92(1.8H,s), 2.99(1.2H,s), 4.36-4.49(1H,m), 4.50-4.57(0.6H,m), 4.78-4.90(0.4H,m), 5.23-5.36(1H,m).

Step 3

(S)-[(N-Cyclobutyl-N-methylcarbamoyl)-[trans-4-(4-nitrobenzenesulfonylamino)cyclohexyl]methyl]carbamic acid tert-butyl ester

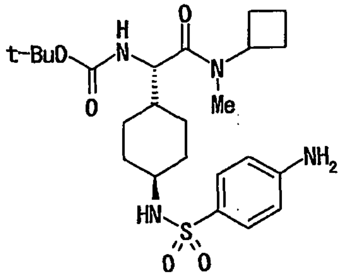


A solution of (S)-[(trans-4-aminocyclohexyl)-(N-cyclobutyl-N-methylcarbamoyl)methyl]carbamic acid tert-butyl ester (1.0 g) obtained in Step 2 and triethylamine (614 μl) in chloroform (10 ml) was cooled to 0°C, and a solution of 4-nitrobenzenesulfonyl chloride (783 mg) in chloroform (5 ml) was added dropwise. The mixture was warmed to room temperature with stirring. The reaction mixture was washed with 5% aqueous citric acid solution and dried over sodium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure and the residue was purified by silica gel chromatography (hexane:ethyl acetate=1:1-2:3) to give the title compound (1.7 g).

^{1}H-NMR(δppm, $CDCl_3$) 0.94-1.22(4H,m), 1.30-1.80(14H,m), 1.80-1.93(2H,m), 1.95-2.35(4H,m), 2.84-3.01(3H,s), 3.05-3.23(1H,m), 4.27-4.55(1.57H,m), 4.59-4.73(0.98H,m), 4.73-4.92(0.50H,m), 5.13-5.35(0.95H,m), 7.99-8.10(2H,d,J=8.8Hz), 8.27-8.40(2H,d,J=8.8Hz).

Step 4

(S)-[[trans-4-(4-Aminobenzenesulfonylamino)cyclohexyl]-(N-cyclobutyl-N-methylcarbamoyl)methyl]carbamic acid tert-butyl ester

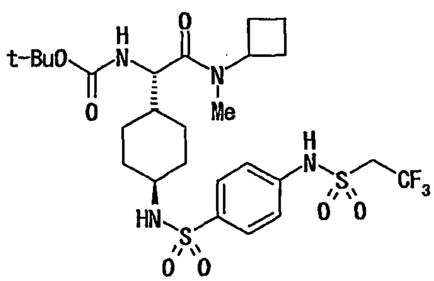


To a solution of (S)-[(N-cyclobutyl-N-methylcarbamoyl)-[trans-4-(4-nitrobenzenesulfonylamino)cyclohexyl]methyl]carbamic acid tert-butyl ester (1.6 g) obtained in Step 3 in ethanol (15 ml), 5% palladium on carbon (300 mg) was added. The mixture was stirred overnight under hydrogen atmosphere. The insoluble material was filtered off through celite, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography (hexane:ethyl acetate=1:3-1:5) to give the title compound (1.376 g).

^{1}H-NMR(δppm, $CDCl_3$) 0.92-1.19(4H,m), 1.21-1.94(16H,m), 1.94-2.32(4H,m), 2.84-3.05(4H,m), 4.11(2H,s), 4.23-4.53(2.66H,m), 4.73-4.88(0.42H,m), 5.18-5.33(0.92H,m), 6.59-6.74(2H,d,J=8.8Hz), 7.53-7.71(2H,d,J=8.8Hz).

Step 5

(S)-[(N-Cyclobutyl-N-methylcarbamoyl)-[trans-4-[4-(2,2,2-trifluoroethanesulfonylamino)benzenesulfonylamino]cyclohexyl]-methyl]carbamic acid tert-butyl ester



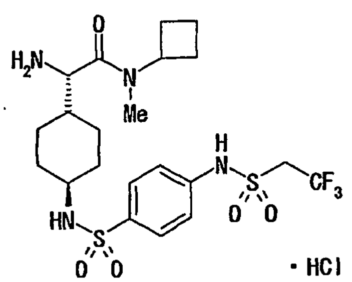
A solution of (S)-[[trans-4-(4-aminobenzenesulfonylamino)cyclohexyl]-(N-cyclobutyl-N-methylcarbamoyl)methyl]carbamic acid tert-butyl ester (150 mg) obtained in Step 4 and pyridine (50 μl) in chloroform (1.5 ml) were cooled to 0°C, and 2,2,2-trifluoroethanesulfonyl chloride (41

μl) was added thereto. The mixture was warmed to room temperature with stirring. The reaction mixture was washed with 5% aqueous citric acid solution and dried over sodium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure and the residue was purified by silica gel chromatography (hexane:ethyl acetate=1:2) to give the title compound (185 mg).

^{1}H-NMR(δppm,$CDCl_3$) 0.97-1.20(4H,m), 1.30-1.92(16H,m), 1.96-2.32(4H,m), 2.85-3.00(3H,s), 3.00-3.14(1H,m), 3.79-3.93(2H,q,J=8.0Hz), 4.30-4.60(2.76H,m), 4.73-4.86(0.36H,m), 5.24-5.38(0.88H,m), 7.29-7.44(2H,d,J=8.8Hz), 7.75-7.94(2H,d,J=8.8Hz).

Step 6

(2S)-2-Amino-N-cyclobutyl-N-methyl-2-[trans-4-[4-(2,2,2-trifluoroethanesulfonylamino)benzenesulfonylamino]cyclohexyl]-acetamide hydrochloride



(S)-[(N-Cyclobutyl-N-methylcarbamoyl)-[trans-4-[4-(2,2,2-trifluoroethanesulfonylamino)benzenesulfonylamino]cyclohexyl]-methyl]carbamic acid tert-butyl ester (185 mg) obtained in Step 5 was suspended in ethyl acetate (4 ml), a solution of 4N-hydrogen chloride in ethyl acetate was added. The mixture was stirred for 2 hrs at room temperature. The reaction mixture was concentrated under reduced pressure and ethyl acetate was added to the residue and the mixture was stirred. The precipitated solid was collected by filteration, washed with ethyl acetate and dried under reduced pressure to give the title compound (132.1 mg).

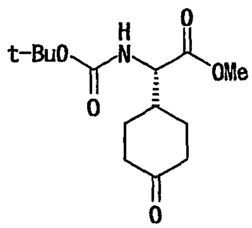
^{1}H-NMR(δppm,DMSO-d_6) 0.88-1.21(4H,m), 1.33-1.76(7H,m), 1.84-2.36(4H,m), 2.67-2.96(4H,m), 3.97-4.10(0.45H,m), 4.14-4.26(0.55H,m), 4.35-4.49(0.55H,m), 4.61-4.78(2.45H,m), 7.27-

7.38(2H,d,J=8.8Hz), 7.54-7.66(1H,m), 7.68-7.78(2H,d,J=8.8Hz), 7.85-8.08(3H,m), 10.88-11.15(1H,s).

Example 33

Step 1

(S)-2-(tert-Butoxycarbonylamino)-2-(4-oxocyclohexyl)acetic acid methyl ester

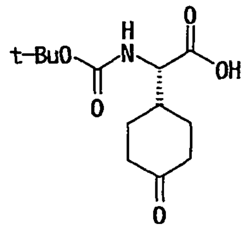


A solution of oxalyl chloride (34.9 ml) in dichloromethane (500 ml) was cooled to -78°C, a solution of dimethyl sulfoxide (56.8 ml) in dichloromethane (100 ml) was added dropwise thereto. The mixture was stirred for 5 min at the same temperature. A solution of (S)-2-(tert-butoxycarbonylamino)-2-(4-hydroxycyclohexyl)acetic acid methyl ester (63 g) synthesized by the method described in WO02/076450 in dichloromethane (300 ml) was added dropwise and the mixture was stirred for 30 min at the same temperature. Triethylamine (250 ml) was added dropwise to the reaction mixture. Water (400 ml) was added at 0°C, and the organic layer was separated, washed successively with 5% aqueous potassium hydrogen sulfate solution and saturated brine, and dried over sodium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure and the residue was purified by silica gel chromatography (hexane:ethyl acetate=3:2-1:1) to give the title compound (45 g).

^{1}H-NMR(δppm,$CDCl_3$) 1.34-1.68(12H,m), 1.83-2.11(2H,m), 2.17-2.51(4H,m), 3.76(3H,s), 4.06-4.17(1H,m), 5.05-5.18(1H,m).

Step 2

(S)-2-(tert-Butoxycarbonylamino)-2-(4-oxocyclohexyl)acetic acid

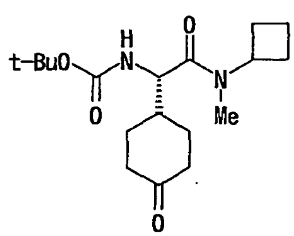


A solution of (S)-2-(tert-butoxycarbonylamino)-2-(4-oxocyclohexyl)acetic acid methyl ester (30 g) obtained in Step 1 in tetrahydrofuran (84 ml) and methanol (84 ml) was cooled to 0°C. 2N aqueous sodium hydroxide solution (84.1 ml) was added dropwise, and the mixture was stirred for 2 hr at room temperature. A mixture of hexane:diethyl ether (1:1) was added to the reaction mixture to be separated, and the aqueous layer was neutralized with 5% aqueous potassium hydrogen sulfate solution and evaporated under reduced pressure. 5% Aqueous potassium hydrogen sulfate solution was added to adjust pH to 1-2, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over sodium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure to give the title compound (29.47 g).

^{1}H-NMR(δppm,$CDCl_3$) 1.25-1.65(11H,m), 1.72-1.94(2H,m), 2.04-2.24(3H,m), 2.24-2.45(2H,m), 3.72-3.82(0.2H,br), 3.88-3.96(0.8H,dd,J=8Hz), 6.70-6.81(0.2H,br), 7.09(0.8H,d,J=8Hz), 12.35-12.80(1H,br).

Step 3

(S)-[(N-Cyclobutyl-N-methylcarbamoyl)-(4-oxocyclohexyl)methyl]carbamic acid tert-butyl ester



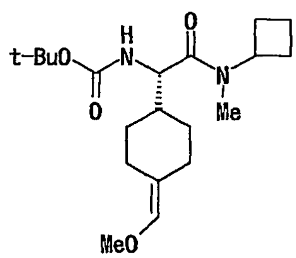
A solution of (S)-2-(tert-butoxycarbonylamino)-2-(4-oxocyclohexyl)acetic acid (29.47 g) obtatned in Step 2 in N,N-dimethylformamide (150 ml) was cooled to 0°C. N-

methylcyclobutylamine hydrochloride (19.1 g) synthesized in accordance with the method described in Journal of Medicinal Chemistry, 1994, 37, 3482, and diisopropylethylamine (35.07 ml) were added, (benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate (59.84 g) was gradually added. After the completion of the addition, the mixture was allowed to warm to room temperature. Water (150 ml) was added and the mixture was extracted with a mixture of ethyl acetate-hexane. The organic layer was washed successively with 5% aqueous potassium hydrogen sulfate solution, saturated aqueous sodium hydrogen carbonate solution, and saturated brine, and dried over sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography (hexane:ethyl acetate=2:3) to give the title compound (23.5 g).

^{1}H-NMR(δppm,$CDCl_3$) 1.23-2.49(24H,m), 2.88-3.09(3H,s), 4.30-4.58(1H,m),4.58-4.75(0.6H,m), 4.76-4.93(0.4H,m), 5.26-5.49(1H,m).

Step 4

(S)-[(N-Cyclobutyl-N-methylcarbamoyl)-(4-methoxymethylenecyclohexyl)methyl]carbamic acid tert-butyl ester



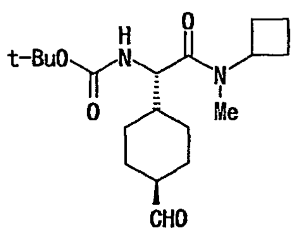
To a solution of (S)-[(N-cyclobutyl-N-methylcarbamoyl)-(4-oxocyclohexyl)methyl]carbamic acid tert-butyl ester (22.10 g) obtained in Step 3 in methanol (180 ml) was added dropwise a solution of dimethyl (1-diazo-2-oxopropyl)phosphonate (19.07 g) in methanol (40 ml) under an argon atmosphere at 0°C. Potassium carbonate (18.08 g) was added by small portions at 0°C and the mixture was stirred at 0°C for 45 min. A saturated aqueous ammonium chloride solution (200 ml) was added to the reaction

mixture at 0°C to adjust the mixture to pH 8. The solvent was evaporated under reduced pressure, and the aqueous layer was extracted with a mixture of hexane:ethyl acetate (1:1). The organic layer was washed with brine, and dried over sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography (hexane:ethyl acetate=2.5:1-1.5:1) to give the title compound (24.93 g).

^{1}H-NMR(δppm,$CDCl_3$) 0.91-2.40(23H,m), 2.70-2.85(1H,m), 2.86-3.05(3H,s), 3.51(3H,s), 4.27-4.62(2.3H,m), 4.77-4.93(0.7H,m), 5.19-5.38(1H,m), 5.68-5.80(1H,m).

Step 5

(S)-[(N-Cyclobutyl-N-methylcarbamoyl)-(trans-4-formylcyclohexyl)methyl]carbamic acid tert-butyl ester



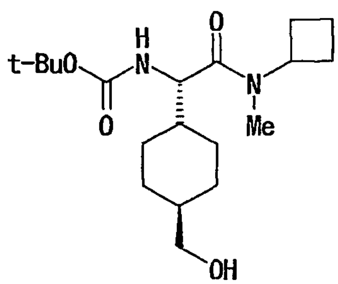
A solution of (S)-[(N-cyclobutyl-N-methylcarbamoyl)-(4-methoxymethylenecyclohexyl)methyl]carbamic acid tert-butyl ester (22.88 g) obtained in Step 4 in dichloromethane (500 ml) was cooled to 0°C under an argon atmosphere. Thereto was added dropwise a solution of trichloroacetic acid (40.80 g) in dichloromethane (150 ml) at 0°C over 15 min and the mixture was stirred at 0°C for 30 min. An aqueous sodium hydrogen carbonate solution was added to the reaction mixture at 0°C to adjust to pH 8 and the organic layer was separated. The organic layer was washed with saturated brine and dried over sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. Of the residue, 13 g was dissolved in acetone (65 ml), 5% aqueous potassium hydrogen sulfate solution (65 ml) was added and the mixture was stirred overnight. The reaction mixture was concentrated under reduced pressure and

separated from ethyl acetate - water. The organic layer was dried over sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The residue was dissolved in water - methanol (1:1), potassium carbonate (16.2 g) was added and the mixture was stirred at room temperature for 1.5 hr. The filtrate was concentrated under reduced pressure and separated from ethyl acetate - water. The organic layer was washed with saturated brine, and dried over sodium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure to give the title compound (10.2 g).

1H-NMR(δppm,$CDCl_3$) 1.09-1.28(4H,m), 1.43(9H,s), 1.53-1.81(7H,m), 2.01-2.31(5H,m), 2.94(1.74H,s), 3.01(1.26H,s), 4.35-4.61(1.58H,m), 4.86(0.42H,m), 5.35(1H,m), 9.60(1H,s).

Step 6

(S)-[(N-Cyclobutyl-N-methylcarbamoyl)-(trans-4-hydroxymethylcyclohexyl)methyl]carbamic acid tert-butyl ester



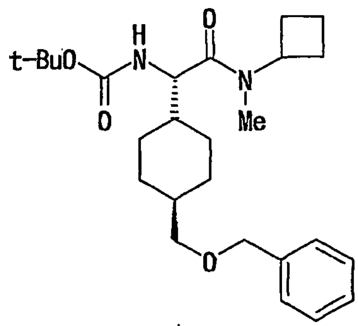
To a solution of (S)-[(N-cyclobutyl-N-methylcarbamoyl)-(trans-4-formylcyclohexyl)methyl]carbamic acid tert-butyl ester (2.11 g) obtained in Step 5 in methanol (20 ml) was added sodium borohydride (227 mg) at 0°C. The mixture was stirred for 2 hr at 0°C. Water (10 ml) and acetic acid (one drop) were added threrto and stirred for 30 min at room temperature. The solvent was evaporated under reduced pressure, and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with saturated brine, and dried over sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure, and the residue was purified by silica gel chromatography (hexane:ethyl acetate=1:1-ethyl acetate) to give

the title compound (1.64 g).

^{1}H-NMR(δppm, $CDCl_3$) 0.82-1.00(2H,m), 1.03-1.12(2H,m), 1.42(9H,s), 1.42-1.50(2H,m), 1.62-1.87(6H,m), 2.06-2.32(4H,m), 2.93(1.6H,s), 3.01(1.4H,s), 3.40-3.46(2H,m), 4.40-4.60(1.6H,m), 4.78-4.90(0.5H,m), 5.25-5.40(0.9H,m).

Step 7

(S)-[(trans-4-Benzyloxymethylcyclohexyl)-(N-cyclobutyl-N-methylcarbamoyl)methyl]carbamic acid tert-butyl ester

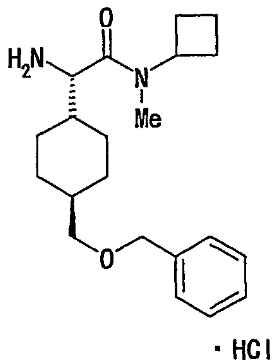


A solution of (S)-[(N-cyclobutyl-N-methylcarbamoyl)-(trans-4-hydroxymethylcyclohexyl)methyl]carbamic acid tert-butyl ester (30 mg) obtained in Step 6, 2,6-di-tert-butyl-4-methylpyridine (21 mg) and silver trifluoromethanesulfonate (24 mg) in dichloromethane (600 μl) was cooled to 0°C, benzyl bromide (11.1 μl) was added thereto, and the mixtrure was stirred for 1 hr at 0°C. The reaction mixture was filtered using celite, and the filtrate was concentrated under reduced pressure. The residue was dissolved in ethyl acetate, washed successively with 10% aqueous citric acid solution, water, saturated aqueous sodium hydrogen carbonate solution, water and saturated brine, and dried over sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure, and the residue was purified by silica gel chromatography (hexane:ethyl acetate=3:1) to give the title compound (28 mg).

^{1}H-NMR(δppm, $CDCl_3$) 0.80-1.19(4H,m), 1.33-1.78(6H,m), 1.42(9H,s), 1.79-1.91(2H,m), 1.98-2.35(4H,m), 2.93(1.73H,s), 3.00(1.27H,s), 3.21-3.29(2H,d,J=6.2Hz), 4.37-4.58(1.58H,m), 4.47(2H,s), 4.79-4.92(0.42H,m), 5.24-5.38(1H,m), 7.22-7.38(5H,m).

Step 8

(2S)-2-Amino-2-(trans-4-benzyloxymethylcyclohexyl)-N-cyclobutyl-N-methylacetamide hydrochloride



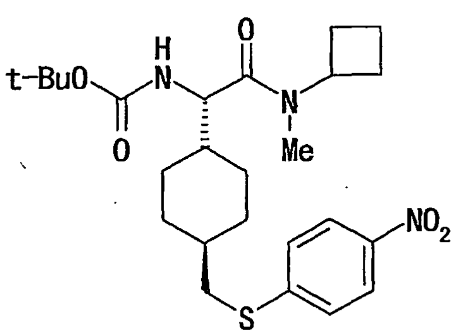
(S)-[(trans-4-Benzyloxymethylcyclohexyl)-(N-cyclobutyl-N-methylcarbamoyl)methyl]carbamic acid tert-butyl ester (28 mg) obtained in Step 7 was dissolved in 4N-hydrogen chloride ethyl acetate solution (1 ml), and the solution was sttired for 1.5 hr at room temperature. The reaction mixture was concentrated under reduced pressure to give the title compound (19 mg).

^{1}H-NMR(δppm,DMSO-d_6) 0.77-1.01(4H,m), 1.36-1.85(8H,m), 1.93-2.36(4H,m), 2.88(1.73H,s), 2.97(1.27H,s), 3.22(2H,d,J=6.2Hz), 4.13(0.42H,d,J=5.8Hz), 4.28(0.58H,d,J=4.8Hz), 4.42(2H,s), 4.47-4.59(0.58H,m), 4.70-4.83(0.42H,m), 7.22-7.38(5H,m), 8.05(3H,brs).

Example 34

Step 1

(S)-[(N-Cyclobutyl-N-methylcarbamoyl)-[trans-4-(4-nitrophenylsulfanylmethyl)cyclohexyl]methyl]carbamic acid tert-butyl ester



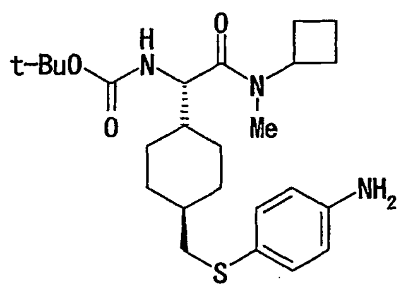
To a solution of (S)-[(N-cyclobutyl-N-methylcarbamoyl)-

(trans-4-hydroxymethylcyclohexyl)methyl]carbamic acid tert-butyl ester (177 mg) obtained in Step 6 of Example 33, 4-nitrothiophenol (0.55 ml) and triphenylphosphine (0.60 ml) in tetrahydrofuran (2 ml), was added diisopropyl azodicarboxylate (0.60 ml) under ice cooling and argon atomosphere. After allowing the reaction mixture to room temperature, the mixture was stirred overnight. The reaction mixture was concentrated under reduced pressure, and the residue was purified by silica gel chromatography (hexane:ethyl acetate=2:1-1:1) to give the title compound (290 mg) as a yellow amorphous form.

^{1}H-NMR(δppm,$CDCl_3$) 0.96-1.20(4H,m), 1.42(9H,s), 1.47-1.79(6H,m), 1.94-2.33(6H,m), 2.88(2H,d,J=6.9Hz), 2.93(1.74H,s), 3.00(1.26H,s), 4.38-4.46(0.42H,m), 4.48-4.61(0.58H,m), 4.79-4.90(0.58H,m), 4.91-5.03(0.42H,m), 5.24-5.38(1H,m), 6.30(1H,brs), 7.28(2H,d,J=8.8Hz), 8.10(2H,d,J=8.8Hz).

Step 2

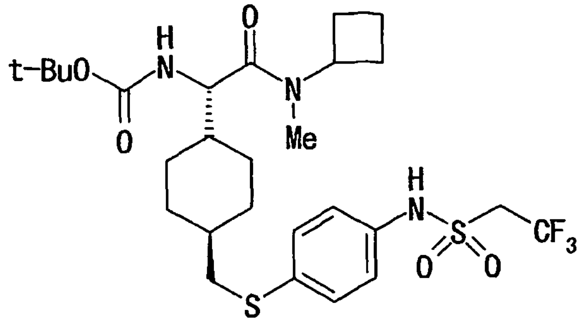
(S)-[[trans-4-(4-Aminophenylsulfanylmethyl)cyclohexyl]-(N-cyclobutyl-N-methylcarbamoyl)methyl]carbamic acid tert-butyl ester



Using (S)-[(N-cyclobutyl-N-methylcarbamoyl)-[trans-4-(4-nitrophenylsulfanylmethyl)cyclohexyl]methyl]carbamic acid tert-butyl ester obtained in Step 1, the title compound was obtained in the same manner as in Step 4 of Example 29.

Step 3

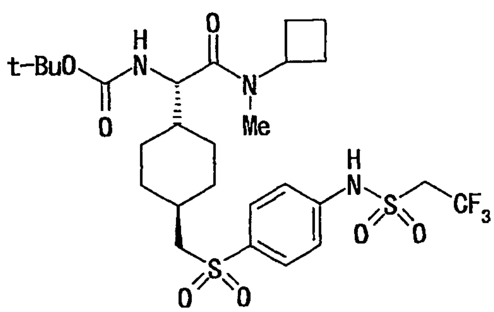
(S)-[(N-Cyclobutyl-N-methylcarbamoyl)-[trans-4-[4-(2,2,2-trifluoroethanesulfonylamino)benzenesulfanylmethyl]cyclohexyl]-methyl]carbamic acid tert-butyl ester



Using (S)-[[trans-4-(4-aminophenylsulfanylmethyl)cyclohexyl]-(N-cyclobutyl-N-methylcarbamoyl)methyl]carbamic acid tert-butyl ester obtained in Step 2, the title compound was obtained in the same manner as in Step 5 of Example 29.

Step 4

(S)-[(N-Cyclobutyl-N-methylcarbamoyl)-[trans-4-[4-(2,2,2-trifluoroethanesulfonylamino)benzenesulfonylmethyl]cyclohexyl]-methyl]carbamic acid tert-butyl ester



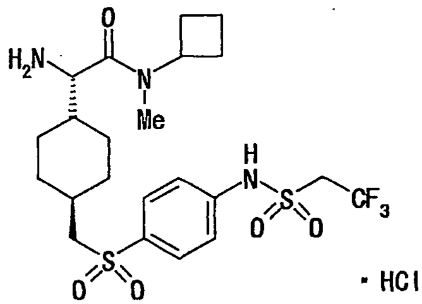
To a solution of (S)-[(N-cyclobutyl-N-methylcarbamoyl)-[trans-4-[4-(2,2,2-trifluoroethanesulfonylamino)-benzenesulfanylmethyl]cyclohexyl]methyl]carbamic acid tert-butyl ester (123 mg) obtained in Step 3 in chloroform (5 ml) was added m-chloroperoxybenzoic acid (110 mg), and the mixture was stirred for 3.5 hr at room temperature. The reaction mixture was diluted with a mixture of chloroform-1M aqueous potassium carbonate solution, and partitioned. The organic layer was washed with saturated brine, and dried over sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure, and the residue was purified by preparative thin layer

chromatography (hexane:ethyl acetate=1:2) to give the title compound (95 mg).

^{1}H-NMR(δppm,$CDCl_3$) 1.01-1.15(4H,m), 1.40-1.76(6H,m), 1.42(4H,s), 1.91-2.28(6H,m), 2.93(1.74H,s), 2.95(2H,d,J=6.9Hz), 3.00(1.26H,s), 3.89(2H,q,J=8.8Hz), 4.35-4.60(1.58H,m), 4.75-4.90(0.42H,m), 5.25-5.35(1H,m), 7.41(2H,d,J=8.6Hz), 7.89(2H,d,J=8.6Hz).

Step 5

(2S)-2-Amino-N-cyclobutyl-N-methyl-2-[trans-4-[4-(2,2,2-trifluoroethanesulfonylamino)benzenesulfonylmethyl]cyclohexyl]-acetamide hydrochloride



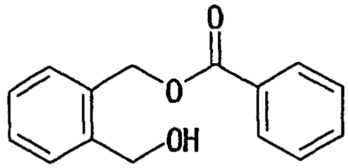
Using (S)-[(N-cyclobutyl-N-methylcarbamoyl)-[trans-4-[4-(2,2,2-trifluoroethanesulfonylamino)benzenesulfonylmethyl]-cyclohexyl]methyl]carbamic acid tert-butyl ester obtained in Step 4, the title compound was obtained in the same manner as in Step 6 of Example 29.

^{1}H-NMR(δppm,DMSO-d_6) 0.94-1.24(4H,m), 1.48-1.72(6H,m), 1.78-1.88(2H,m), 1.96-2.39(4H,m), 2.87(1.74H,s), 2.96(1.26H,s), 3.17(2H,d,J=6.0Hz), 4.11(0.42H,brs), 4.25(0.58H,brs), 4.50(0.58H,m), 4.74(2H,q,J=9.7Hz), 4.70-4.87(0.42H,m), 7.40(2H,d,J=8.6Hz), 7.83(2H,d,J=8.6Hz), 8.02(3H,brs), 11.17(1H,brs).

Example 212

Step 1

2-(Benzoyloxymethyl)benzyl alcohol

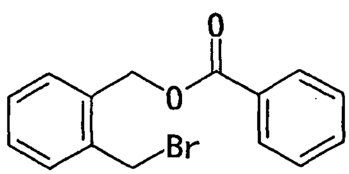


1,2-Benzenedimethanol (5.00 g) was dissolved in tetrahydrofuran (60ml), and triethylamine (4.20 ml) and benzoyl chloride (5.04 ml) were added dropwise thereto under cooling. After stirring for 2 hr at room temperature, the reaction mixture was poured into water, and extracted with ethyl acetate. The organic layer was washed successively with saturated aqueous sodium hydrogen carbonate solution, water and saturated brine, and dried over sodium sulfate. The drying agent was filtered off, and filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography (hexane:ethyl acetate=1:2-1:3) to give the title compound (4.49 g).

^{1}H-NMR(δppm, $CDCl_3$) 2.13(1H, brs), 4.86(2H, s), 5.51(2H, s), 7.33-7.59 (7H, m), 8.06(2H, d, J=4.6Hz).

Step 2

2-(Benzoyloxymethyl)benzyl bromide

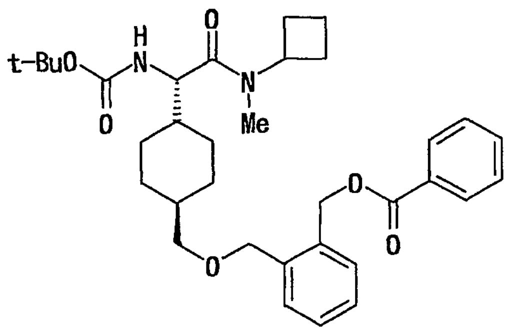


2-(Benzoyloxymethyl)benzyl alcohol (4.49 g) was dissolved in chloroform (45 ml), and triphenylphosphine (5.34 g) and carbon tetrabromide (6.76 g) was added thereto under ice-cooling. After stirring for 1 hr at room temperature, the reaction mixture was concentrated under reduced pressure, and the residue purified by silica gel chromatography (hexane:ethyl acetate=9:1) to give the title compound (5.08 g).

^{1}H-NMR(δppm, $CDCl_3$) 4.67(2H, s), 5.53(2H, s), 7.34-7.60(7H, m), 8.08(2H, d, J=7.6Hz).

Step 3

(S)-[(trans-4-[2-(Benzoyloxymethyl)benzyloxymethyl]cyclohexyl)-(N-cyclobutyl-N-methylcarbamoyl)methyl]carbamic acid tert-butyl ester

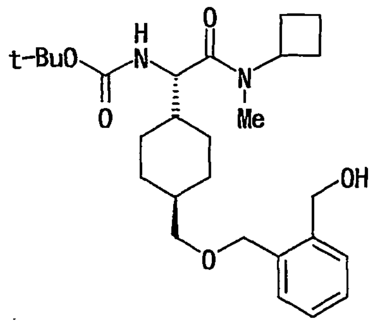


To a solution of (S)-[(N-cyclobutyl-N-methylcarbamoyl)-(trans-4-hydroxymethylcyclohexyl)methyl]carbamic acid tert-butyl ester (4.00 g) obtained in Step 6 of Example 33 and 2,6-di-tert-butyl-4-methylpyridine (2.78 g) in chloroform (40 ml) was added dropwise a solution of 2-(benzoyloxymethyl)benzylbromide (3.78 g) in chloroform (40 ml) under ice-cooling, and then silver trifluoromethanesulfonate (3.19 g) was added. After stirring for 1 hr at room temperature, the insoluble substance was filtered off using celite, and the filtrate was concentrated under reduced pressure. Diethyl ether (50 ml) was added to the residue, the insoluble substance was filtered off, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography (hexane:ethyl acetate=3:1-2:1) to give the title compound (4.89 g).

^{1}H-NMR(δppm, $CDCl_3$) 0.87-1.23(4H, m), 1.43(9H, s), 1.51-1.73(10H, m), 1.80-1.85(2H, m), 2.08-2.28(4H, m), 2.93(1.7H, s), 3.00(1.3H, s), 3.28(2H, t, J=3.2Hz), 4.40-4.56(1H, m), 4.61(2H, s), 4.86(0.4H, t, J=9.0Hz), 5.30(0.7H, dd, J=14.4Hz, 9.3Hz), 5.45(2H, s), 7.31-7.59(7H, m), 8.06-8.08(2H, m).

Step 4

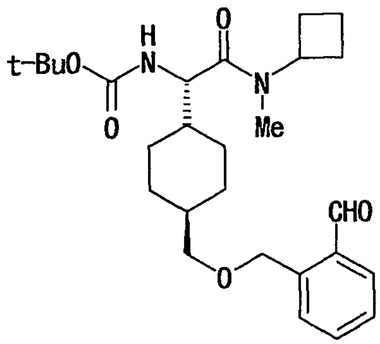
(S)-[(trans-4-[2-(Hydroxymethyl)benzyloxymethyl]cyclohexyl)-(N-cyclobutyl-N-methylcarbamoyl)methyl]carbamic acid tert-butyl ester



To a solution of (S)-[(trans-4-[2-(benzoyloxymethyl)benzyloxymethyl]cyclohexyl)-(N-cyclobutyl-N-methylcarbamoyl)methyl]carbamic acid tert-butyl ester (4.89 g) obtained in Step 3 in tetrahydrofuran (24 ml) and methanol (24 ml) was added dropwise 1N aqueous sodium hydroxide solution (16.9 ml) at room temperature, and the mixture was stirred for 30 min at room temperature. The reaction mixture was poured into saturated aqueous sodium hydrogen carbonate solution and extracted with ethyl acetate. The organic layer was washed successively with saturated aqueous sodium hydrogen carbonate solution and saturated brine, and dried over sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography (hexane:ethyl acetate=1:1-2:3) to give the title compound (3.76 g). ^{1}H-NMR(δppm, $CDCl_3$) 0.85-1.18(4H, m), 1.42(9H, s), 1.62-1.73(4H, m), 1.76-1.82(2H, m), 2.01-2.29(6H, m), 2.92(1.7H, s), 2.97(1.3H, s), 3.24(1H, brs), 3.30-3.33(2H, m), 4.40-4.55(1H, m), 4.58(2H, s), 4.65(2H, s), 4.84(0.3H, q, J=8.6Hz), 5.30(0.7H, dd, J=14.6Hz, 9.5Hz), 7.30-7.40(4H, m).

Step 5

(S)-[(trans-4-[2-Formylbenzyloxymethyl]cyclohexyl)-(N-cyclobutyl-N-methylcarbamoyl)methyl]carbamic acid tert-butyl ester

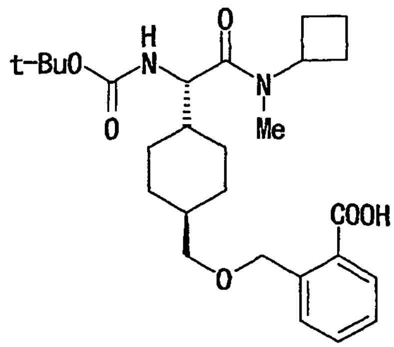


To a mixture of (S)-[(trans-4-[2-(hydroxymethyl)benzyloxymethyl]cyclohexyl)-(N-cyclobutyl-N-methylcarbamoyl)methyl]carbamic acid tert-butyl ester (3.76 g) obtained in Step 4, molecular sieves 4Å (1.4 g) and chloroform (38 ml) was added successively N-methylmorpholine N-oxide (1.39 g) and tetrapropylammonium perruthenate (139 mg) under ice-cooling. After stirring for 1 hr at room temperature, the insoluble substance was filtered off, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography (hexane:ethyl acetate=2:1-3:2) to give the title compound (2.92 g).

^{1}H-NMR(δppm, $CDCl_3$) 0.88-1.17(5H, m), 1.42(9H, s), 1.63-1.72(5H, m), 1.85(2H, d, J=13.0Hz), 2.08-2.31(4H, m), 2.93(1.7H, s), 3.01(1.3H, s), 3.36(2H, d, J=6.0Hz), 4.49-4.58(2H, m), 4.88(2H, s), 5.32(1H, t, J=11.8Hz), 7.46(1H, t, J=7.4Hz), 7.57-7.63(2H, m), 7.86(1H, d, J=7.4Hz), 10.21(1H, s).

Step 6

2-{trans-4-[(S)-tert-Butoxycarbonylamino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxymethyl}benzoic acid

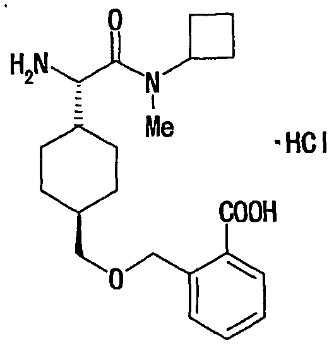


To a solution of (S)-[(trans-4-[2-formylbenzyloxymethyl]cyclohexyl)-(N-cyclobutyl-N-methylcarbamoyl)methyl]carbamic acid tert-butyl ester (2.92 g) obtained in Step 5 in tetrahydrofuran (45 ml) was added a solution of sulfamic acid (780 mg) in water (9 ml) at room temperature. After cooling with ice-bath, a solution of sodium chlorite (726 mg) in water (9 ml) solution was added dropwise over about 5 min to the reaction mixture. After stirring for 10 min at 0°C, sodium sulfite (1.2 g) was added to the reaction mixture. The mixture was stirred for 15 min and poured into water and extracted with ethyl acetate. The organic layer was washed successively with water and saturated brine, and dried over sodium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography (chloroform:methanol=10:1) to give the title compound (2.98 g).

^{1}H-NMR(δppm, $CDCl_3$) 0.90-1.21(4H, m), 1.43(9H, s), 1.60-1.75(6H, m), 1.87(2H, d, J=11.6Hz), 2.05-2.31(4H, m), 2.94(1.7H, s), 3.02(1.3H, s), 3.38(2H, d, J=6.0Hz), 4.26-4.63(1H, m), 4.80-4.85(2H, m), 5.40-5.47(1H, m), 7.38-7.42(1H, m), 7.52-7.61(2H, m), 8.06(1H, t, J=3.9Hz).

Step 7

2-{trans-4-[(S)-Amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxymethyl}benzoic acid hydrochloride



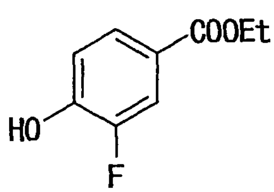
2-{trans-4-[(S)-tert-Butoxycarbonylamino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxymethyl}benzoic acid (2.98 g) obtained in Step 6 was dissolved in a solution of 4N-hydrogen chloride in ethyl acetate (15 ml), and the solution was stirred for 45 min at room temperature. Ethyl acetate (150 ml) was added thereto and the mixture was stirred for 40 min. The solid was collected by filtration and dried under reduced pressure to give the title compound (2.14 g).

^{1}H-NMR(δppm, DMSO-d_6) 0.88-1.21(4H, m), 1.40-1.70(7H, m), 1.79(2H, brs), 1.99-2.30(4H, m), 2.88(1.8H, s), 2.97(1.2H, s), 3.27(2H,d,J=6.0Hz), 4.14(0.4H, brs), 4.52(0.6H, brs), 4.52(0.6H, t, J=8.6Hz), 4.70-4.80(2.4H, m), 7.34-7.38(1H, m), 7.51-7.63(2H, m), 7.82(1H, d, J=7.9Hz), 8.05(3H, brs).

Example 238

Step 1

3-Fluoro-4-hydroxybenzoic acid ethyl ester



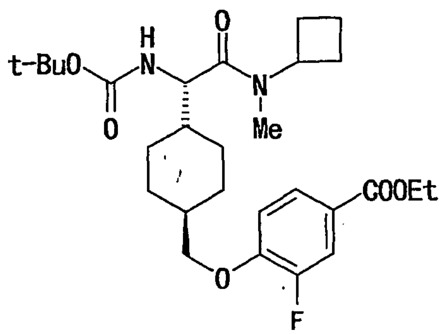
To a solution of 3-fluoro-4-hydroxybenzoic acid (300 mg) in ethanol (3 ml) was added a several drop of concentrated sulfuric acid under an argon atmosphere, and the mixture was refluxed under heating for 5 hr. The reaction mixture was poured into water, and extracted with ethyl acetate. The organic layer was washed with saturated aqueous sodium hydrogen carbonate solution.

and dried over magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure to give the title compound (337 mg) as a white solid.

^{1}H-NMR (δppm, DMSO-d_6) 1.29(3H, t, J=7.0Hz), 4.26(2H, q, J=7.0Hz), 7.04(1H, t, J=8.6Hz), 7.61-7.64(1H, m), 7.66(1H, s), 10.83(1H, brs).

Step 2

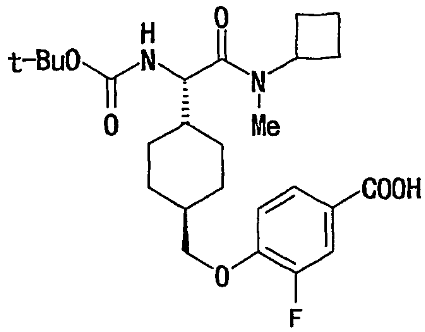
4-{trans-4-[(S)-tert-Butoxycarbonylamino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxy}-3-fluorobenzoic acid ethyl ester



To a solution of (S)-[(N-cyclobutyl-N-methylcarbamoyl)-(trans-4-hydroxymethylcyclohexyl)methyl]carbamic acid tert-butyl ester (70 mg) obtained in Step 6 of Example 33 in tetrahydrofuran (700 μl) was added 3-fluoro-4-hydroxybenzoic acid ethyl ester (44 mg), triphenylphosphine (62 mg) and diisopropyl azodicarboxylate (46.5 μl) under an argon atmosphere. After stirring for about 1.5 hr at room temperature, the mixture was concentrated under reduced pressure, and the residue was purified by silica gel chromatography (hexane:ethyl acetate=4:1-3:1) to give the title compound (122 mg) as a colorless oil.

Step 3

4-{trans-4-[(S)-tert-Butoxycarbonylamino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxy}-3-fluorobenzoic acid

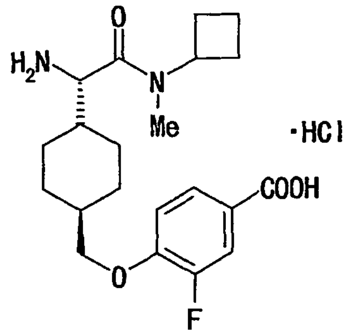


To a solution of 4-{trans-4-[(S)-tert-butoxycarbonylamino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxy}-3-fluorobenzoic acid ethyl ester (122.2 mg) obtained in Step 2 in tetrahydrofuran (1 ml) and methanol (1 ml) was added dropwise 1N aqueous sodium hydroxide solution (936 μl) under an argon atmosphere, the mixture was stirred overnight at room temperature. 5% Aqueous potassium hydrogen sulfate solution was added to the reaction mixture to adjust to pH 2-3. The reaction mixture was extracted with ethyl acetate, and the organic layer was washed with brine and dried over magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography (hexane:ethyl acetate=2:1-chloroform:methanol=40:1-10:1) to give the title compound (88 mg) as white amorphous.

^{1}H-NMR(δppm, $CDCl_3$) 0.95-1.30(4H, m), 1.43(9H, s), 1.50-1.89(6H, m), 1.91-2.01(2H, m), 2.03-2.36(4H, m), 2.95(1.74H, s), 3.03(1.26H, s), 3.88(2H, d, J=9.0Hz), 4.35-4.65(1.58H, m), 4.78-4.95(0.42H, m), 5.31-5.47(1H, m), 6.96(1H, t, J=7.5Hz), 7.78(1H, dd, J=3.0Hz, 12.0Hz), 7.84(1H, d, J=9.0Hz),

Step 4

4-{trans-4-[(S)-Amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxy}-3-fluorobenzoic acid hydrochloride



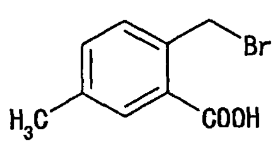
4-{trans-4-[(S)-tert-Butoxycarbonylamino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxy}-3-fluorobenzoic acid (88 mg) obtained in Step 3 was dissolved in 4N-hydrogen chloride ethyl acetate solution (1 ml), and the mixture was stirred for 6 hr at room temperature. The reaction mixture was concentrated under reduced pressure, and diethyl ether was added to the residue. The precipitated solid was collected by filteration, and drying under vacuum to give the title compound (63.5 g).

^{1}H-NMR (δppm, DMSO-d_6) 0.94-1.34(4H, m), 1.54-1.79(6H, m), 1.81-1.94(2H, m), 1.97-2.37(4H, m), 2.90(1.71H, s), 2.99(1.29H, s), 3.94(2H, d, J=6.0Hz), 4.11-4.19(0.43H, m), 4.27-4.34(0.57H, m), 4.47-4.61(0.57H, m), 4.70-4.85(0.43H, m), 7.25(1H, t, J=9.0Hz), 7.66(1H, dd, J=3.0Hz, 12.0Hz), 7.74(1H, d, J=9.0Hz), 8.11(3H, brs).

Example 242

Step 1

2-Bromomethyl-5-methylbenzoic acid

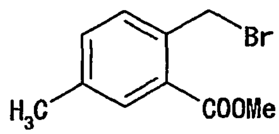


To a solution of 2,5-dimethylbenzoic acid (10.0 g) in carbon tetrachloride (200 ml), were added N-bromosuccinimide (12.45 g) and benzoyl peroxide (1.0 g) under an argon atmosphere, and the mixture was heated under reflux for 1 hr. The insoluble material was filtered off and washed with carbon tetrachloride (50 ml). About 125 ml of the solvent was evaporated from the filtrate, and the concentrated solution was stirred for 3.5 hr at room temperature. The precipitated solid was collected by filtration.

and dried under reduced pressure to give the title compound (5.48 g) as a white solid.

Step 2

2-Bromomethyl-5-methylbenzoic acid methyl ester

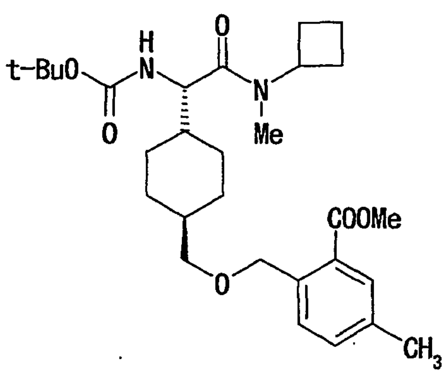


To a solution of 2-bromomethyl-5-methylbenzoic acid (4.59 g) obtained in Step 1 in tetrahydrofuran (100 ml) and methanol (40ml), was added dropwise 2M trimethylsilyl diazomethane-hexane solution (11 ml) over 10 min under an argon atmosphere. After stirring for 3.5 hr at room temperature, acetic acid was added dropwise to the reaction mixture until the color (yellow) of the mixture disappeared. The reaction mixture was concentrated under reduced pressure, and the residue was purified by silica gel chromatography (hexane:ethyl acetate=100:1) to give the title compound (3.40 g) as a colorless oil.

^{1}H-NMR(δppm, $CDCl_3$) 2.38(3H, s), 3.94(3H, s), 4.93(2H, s), 7.30(1H, d, J=9.0Hz), 7.35(1H, d, J=9.0Hz), 7.78(1H, s).

Step 3

2-{trans-4-[(S)-tert-Butoxycarbonylamino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxymethyl}-5-methylbenzoic acid methyl ester



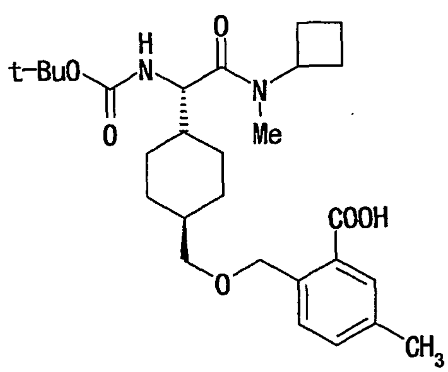
To a solution of (S)-[(N-cyclobutyl-N-methylcarbamoyl)-(trans-4-hydroxymethylcyclohexyl)methyl]carbamic acid tert-butyl ester (1.00 g) obtained in Step 6 of Example 33 and 2-bromomethyl-

5-methylbenzoic acid methyl ester (1.23 g) in dichloromethane (15 ml), were added 2,6-di-tert-butyl-4-methylpyridine (955 mg, 4.7 mmol) and silver trifluoromethanesulfonate (1.20 g, 4.7 mmol) under ice-cooling and an argon atmosphere. After stirring for 2 hr under ice-cooling, the mixture was stirred for 2.5 hr at room temperature. The insoluble material was filtered off, and the filtrate was concentrated under reduced pressure. Diethyl ether was added to the residue, and the insoluble material was filtered off. The filtrate was concentrated under reduced pressure, and the residue was purified by silica gel chromatography (hexane:ethyl acetate=5:1-4:1-3:1) to give the title compound (851 mg).

^{1}H-NMR(δppm, $CDCl_3$) 0.79-1.24(4H, m), 1.42(9H, s), 1.58-1.78(6H, m), 1.80-1.92(2H, m), 2.01-2.32(4H, m), 2.36(3H, s), 2.93(1.77H, s), 3.01(1.23H, s), 3.31(2H, d, J=9.0Hz), 3.87(3H, s), 4.36-4.60(1.59H, m), 4.80(2H, s), 4.82-4.95(0.41H, m), 5.23-5.38(1H, m), 7.32(1H, d, J=9.0Hz), 7.51(1H, d, J=9.0Hz), 7.72(1H, s).

Step 4

2-{trans-4-[(S)-tert-Butoxycarbonylamino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxymethyl}-5-methylbenzoic acid



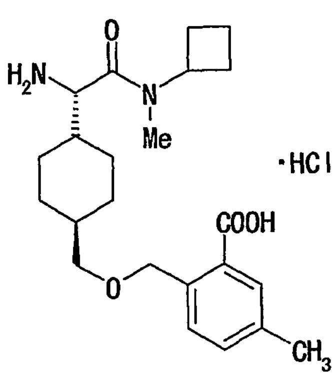
A solution of 2-{trans-4-[(S)-tert-butoxycarbonylamino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxymethyl}-5-methylbenzoic acid methyl ester (851mg) obtained in Step 3 in tetrahydrofuran (4.3 ml) and methanol (4.3 ml) was cooled under ice-bath, and 2N aqueous sodium hydroxide solution (3.30ml) was added dropwise thereto under an argon atmosphere, and the mixture

was stirred overnight at room temperature. The reaction mixture was cooled under ice-bath, and after adding 1N hydrochloric acid (6.6 ml), 5% aqueous potassium hydrogen sulfate was further added to the reaction mixture to adjust pH to 2. The mixture was extracted with ethyl acetate, and the organic layer was washed with saturated brine and dried over magnesium sulfate. The drying agent was filtered off, and the filtrate was concentration under reduced pressure. The residue was purified by silica gel chromatography (hexane:ethyl acetate=2:1-1:1) to give the title compound (702 mg) as white amorphous.

^{1}H-NMR (δppm, $CDCl_3$) 0.84-1.22(4H, m), 1.42(9H, s), 1.48-1.78(6H, m), 1.79-1.91(2H, m), 2.01-2.32(4H, m), 2.39(3H, s), 2.93(1.75H, s), 3.01(1.25H, s), 3.36(2H, d, J=6.0Hz), 4.38-4.60(1.58H, m), 4.74(2H, s), 4.77-4.93(0.42H, m), 5.31-5.43(1H, m), 7.33(1H, d, J=9.0Hz), 7.38(1H, d, J=9.0Hz), 7.87(1H, s).

Step 5

2-{trans-4-[(S)-Amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxymethyl}-5-methylbenzoic acid hydrochloride



2-{trans-4-[(S)-tert-Butoxycarbonylamino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxymethyl}-5-methylbenzoic acid (702 mg) obtained in Step 4 was dissolved in a solution (7 ml) of 4N-hydrogen chloride in ethyl acetate under ice-cooling, and the mixture was stirred for 1.5 hr at room temperature. The reaction mixture was concentrated under reduced pressure, and a mixed solution of diethyl ether-ethyl acetate (3:1) was added

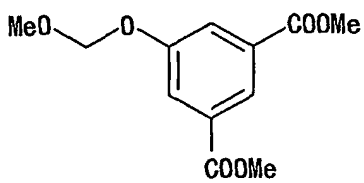
thereto. The precipitated solid was collected by filtration and dried under reduced pressure to give the title compound (545 mg) as a white solid.

^{1}H-NMR(δppm, DMSO-d_6) 0.81-1.02(2H, m), 1.03-1.28(2H, m), 1.37-1.73(6H, m), 1.74-1.87(2H, m), 1.94-2.38(4H, m), 2.33(3H, s), 2.89(1.68H, s), 2.98(1.32H, s), 3.26(2H, d, J=6.0Hz), 4.10-4.18(0.44H, m), 4.25-4.32(0.56H, m), 4.42-4.62(0.56H, m), 4.66-4.85(0.44H, m), 4.71(2H, s), 7.36(1H, d, J=6.0Hz), 7.45(1H, d, J=6.0Hz), 7.64(1H, s), 8.17(3H, brs).

Example 297

Step 1

5-Methoxymethoxyisophthalic acid dimethyl ester

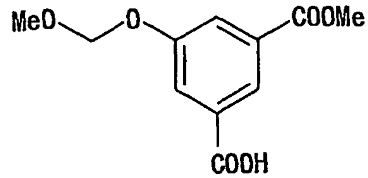


To a solution of 5-hydroxyisophthalic acid dimethyl ester (5.00 g) in N,N-dimethylformamide (25 ml), was added potassium carbonate (4.27 g), and then methoxymethyl chloride (1.99 ml) was added dropwise under ice-cooling. After stirring for 2.5 hr at room temperature, the reaction mixture was poured into water and extracted with ethyl acetate. The organic layer was washed successively with water and brine, and dried over sodium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography (hexane:ethyl acetate=3:1-2:1) to give the title compound (4.21g).

^{1}H-NMR(δppm, $CDCl_3$) 8.34(1H, s), 7.88(2H, d, J=1.5Hz), 5.25(2H, s), 3.94(6H, s), 3.49(3H, s).

Step 2

3-Methoxycarbonyl-5-methoxymethoxybenzoic acid

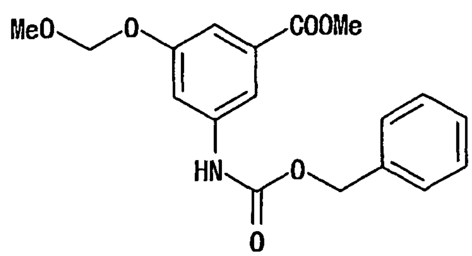


To a solution of 5-methoxymethoxyisophthalic acid dimethyl ester (4.21 g) obtained in Step 1 in tetrahydrofuran (15 ml) and methanol (35 ml), was added aqueous solution of lithium hydroxide monohydrate (695 mg), and the mixture was stirred for 1 hr at room temperature. The reaction mixture was concentrated under reduced pressure, and diethyl ether and water were added to the residue, and partitioned. 5% Aqueous potassium hydrogen sulfate solution was added to the aqueous layer to adjust pH to 2-3. The precipitated crystals were collected by filtration, washed with water and dried to give the title compound (2.90 g).

^{1}H-NMR (δppm, $CDCl_3$) 8.41(1H, s), 7.94(2H, d, J=1.5Hz), 5.27(2H, s), 3.96(3H, s), 3.50(3H, s).

Step 3

3-Benzyloxycarbonylamino-5-methoxymethoxybenzoic acid methyl ester

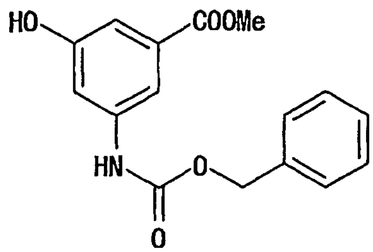


To a solution of 3-methoxycarbonyl-5-methoxymethoxybenzoic acid (890 mg) obtained in Step 2 in tetrahydrofuran (4 ml) and toluene (15 ml), was added triethylamine (1.03 ml) and then diphenylphosphoryl azide (0.959 ml) was added dropwise under ice-cooling. After stirring for 1 hr at room temperature, the mixture was heated for 1 hr at 80°C. Benzyl alcohol was added dropwise to the reaction mixture and the mixture was further heated for 2 hr. The reaction mixture was concentrated under reduced pressure, and the residue was purified by silica gel chromatography (hexane:ethyl acetate=3:1) to give the title compound (645 mg).

^{1}H-NMR(δppm, $CDCl_3$) 7.58(1H, s), 7.50(1H, s), 7.43-7.34(6H, m), 6.76(1H, s), 5.22(2H, s), 5.21(2H, s), 3.90(3H, s), 3.49(3H, s).

Step 4

3-Benzyloxycarbonylamino-5-hydroxybenzoic acid methyl ester

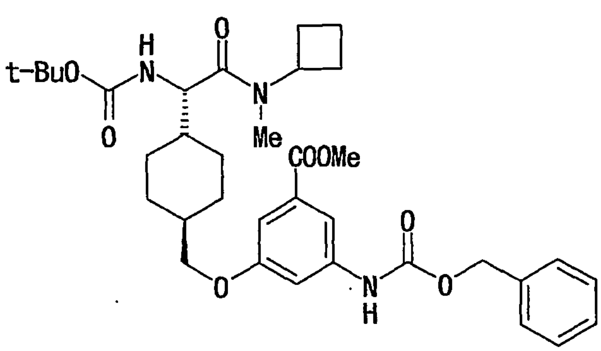


To 3-benzyloxycarbonylamino-5-methoxymethoxybenzoic acid methyl ester (200 mg) obtained in Step 3 was added a solution (2 ml) of 4N-hydrogen chloride in 1,4-dioxane, and the mixture was stirred for 20 min at room temperature. The reaction mixture was concentrated under reduced pressure, and toluene was added to the residue. The solution was concentrated under reduced pressure and dried to give the title compound (175 mg).

^{1}H-NMR(δppm, DMSO-d_6) 9.87(1H, s), 9.80(1H, s), 7.58(1H, s), 7.41-7.35(5H, m), 7.22(1H, t, J=2.3Hz), 6.99 (1H, t, J=1.7Hz), 5.15(2H, s), 3.81(3H, s).

Step 5

3-Benzyloxycarbonylamino-5-{trans-4-[(S)-tert-butoxycarbonylamino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxy}benzoic acid methyl ester



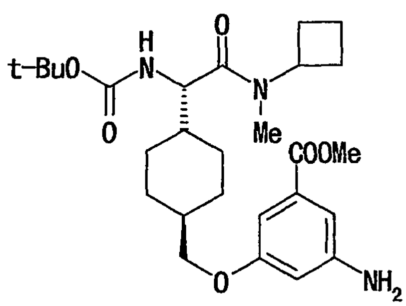
To a solution of (S)-[(N-cyclobutyl-N-methylcarbamoyl)-(trans-4-hydroxymethylcyclohexyl)methyl]carbamic acid tert-butyl

ester (141 mg) obtained in Step 6 of Example 33, 3-benzyloxycarbonylamino-5-hydroxybenzoic acid methyl ester (100 mg) obtained in Step 4 and triphenylphosphine (113 mg) in tetrahydrofuran (2 ml), was added diisopropyl azodicarboxylate (85.1 μl) under ice-cooling. After stirring for 3.5 hr at room temperature, the reaction mixture was concentrated under reduced pressure, and the residue was purified by silica gel chromatography (hexane:ethyl acetate=2:1-3:2) to give the title compound (162 mg).

^{1}H-NMR(δppm, $CDCl_3$) 7.39-7.36(7H, m), 7.27-7.23(1H, m), 6.74(1H, s), 5.34(1H, t, J=8.7Hz), 5.19 (2H, d, J=7.5Hz), 4.87 (0.41H, t, J=8.7Hz), 4.60-4.42(1.59H, m), 3.89(3H, s), 3.77(2H, d, J=6.0Hz), 3.03(1.22H, s), 2.96(1.78H, s), 2.31-2.08(4H, m), 1.92(2H, d, J=11.7Hz), 1.75-1.63(4H, m), 1.62-1.38(2H, m), 1.43(9H, s), 1.28-0.98(4H, m).

Step 6

3-Amino-5-{trans-4-[(S)-tert-butoxycarbonylamino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxy}benzoic acid methyl ester

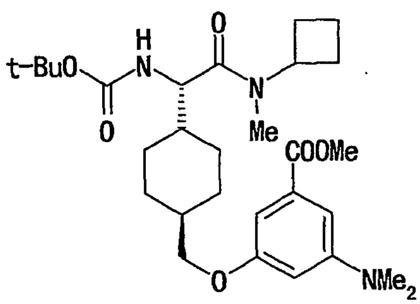


To a solution of 3-benzyloxycarbonylamino-5-{trans-4-[(S)-tert-butoxycarbonylamino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxy}benzoic acid methyl ester (162 mg) obtained in Step 5 in methanol (5 ml), added 5% palladium on carbon (16 mg), and the mixture was stirred under ambient hydrogen atmosphere for 1.5 hr at room temperature. The reaction mixture was filtered through celite, and the filtrate was concentrated under reduced pressure to give the title compound (119 mg).

^{1}H-NMR(δppm, $CDCl_3$) 6.95-6.94(2H, m), 6.39(1H, t, J = 2.1 Hz), 5.33(1H, t, J = 9.2 Hz), 4.87(0.59H, t, J = 8.5 Hz), 4.56-4.46(1.41H, m), 3.87(3H, s), 3.71(2H, t, J = 10.0 Hz), 3.02(1.22H, s), 2.94(1.78H, s), 2.27-2.14(4H, m), 1.89(2H, t, J = 14.1 Hz), 1.73(4H, q, J = 8.9 Hz), 1.53-1.46(2H, m), 1.43(9H, s), 1.19-1.08(4H, m).

Step 7

3-{trans-4-[(S)-tert-Butoxycarbonylamino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxy}-5-dimethylaminobenzoic acid methyl ester



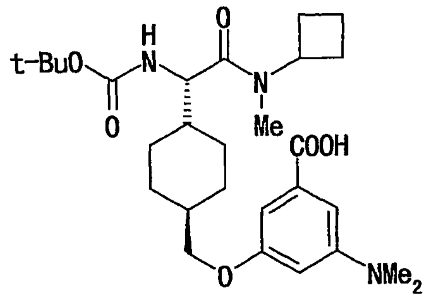
To a solution of 3-amino-5-{trans-4-[(S)-tert-butoxycarbonylamino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxy}benzoic acid methyl ester (119 mg) obtained in Step 6 in acetonitrile (38ml), were added 37% aqueous formaldehyde solution (0.105 ml) and sodium triacetoxyborohydride (312 mg) under ice-cooling, and the mixture was stirred for 30 min at room temperature. After filtrating off the insoluble material, the filtrate was concentrated under reduced pressure. Saturated aqueous sodium hydrogen carbonate solution and ethyl acetate were added to the residue, and partitioned. The organic layer was washed with saturated brine and dried over sodium sulfate. The drying agent was filtrated off and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography (hexane:ethyl acetate=2:1) to give the title compound (123 mg).

^{1}H-NMR(δppm, $CDCl_3$) δ: 7.04(1H, s), 6.89(1H, s), 6.41(1H, t, J=2.4Hz), 5.33(1H, t, J=10.0Hz), 4.87(0.40H, t, J=9.2Hz), 4.58-

4.45(1.60H, m), 3.89(3H, s), 3.77(2H, d, J=6.4Hz), 3.02(1.21H, s), 2.96(6H, s), 2.94(1.79H, s), 2.31-2.13(4H, m), 1.95(2H, d, J=11.7Hz), 1.74-1.50(6H, m), 1.40(9H, s), 1.28-1.09(4H, m).

Step 8

3-{trans-4-[(S)-tert-Butoxycarbonylamino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxy}-5-dimethylaminobenzoic acid

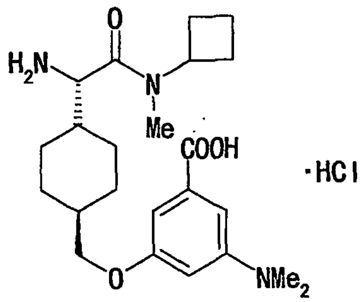


To a solution of 3-{trans-4-[(S)-tert-butoxycarbonylamino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxy}-5-dimethylaminobenzoic acid methyl ester (123 mg) obtained in Step 7 in tetrahydrofuran (0.5 ml) and methanol (1 ml), was added dropwise 4N aqueous sodium hydroxide solution (0.22 ml), and the mixture was stirred overnight at room temperature. The reaction mixture was concentrated under reduced pressure, and diethyl ether and water were added to the residue, and partitioned. The aqueous layer was washed with diethyl ether, and 5% aqueous potassium hydrogen sulfate solution (2.5 ml) was added thereto to adjust pH to 4-6, and extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure to give the title compound (120 mg).

^{1}H-NMR(δppm, $CDCl_3$) 7.09(1H, s), 6.93(1H, d, J=10.9Hz), 6.44(1H, t, J=2.1Hz), 5.40(1H, t, J=7.2Hz), 4.87(0.42H, t, J=8.7Hz), 4.61-4.43(1.58H, m), 3.78(2H, d, J=6.0Hz), 3.03(1.26H, s), 2.97(6H, s), 2.95(1.74H, s), 2.27-2.15(4H, m), 1.95(2H, d, J=11.3Hz), 1.64-1.43(6H, m), 1.43(9H, s), 1.19-1.09(4H, m).

Step 9

3-{trans-4-[(S)-Amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxymethyl}-5-dimethylaminobenzoic acid hydrochloride



3-{trans-4-[(S)-tert-Butoxycarbonylamino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxy}-5-dimethylaminobenzoic acid (60 mg) obtained in Step 8 was dissolved a solution (2 ml) of 4N-hydrogen chloride in ethyl acetate under ice-cooling, and the mixture was stirred for 1.5 hr at room temperature. The reaction mixture was concentrated under reduced pressure, and diethyl ether was added thereto. The precipitated solid was collected by filtration and dried under reduced pressure to give the title compound (45 mg).

^{1}H-NMR (δppm, DMSO-d_6) 8.05 (3H, s), 6.92 (1H, s), 6.78 (1H, s), 6.44 (1H, s), 4.77 (0.45H, t, J = 7.9 Hz), 4.44-4.24 (1.55H, m), 3.79 (2H, d, J = 6.0 Hz), 2.99 (1.35H, s), 2.92 (6H, s), 2.90 (1.65H, s), 2.27-1.97 (4H, m), 1.91-1.85 (2H, m), 1.73-1.67 (6H, m), 1.28-0.98 (4H, m).

The following compounds were obtained in the same manner as in Examples 1, 29, 33, 34, 212, 238, 242 and 297.

Table 1-1

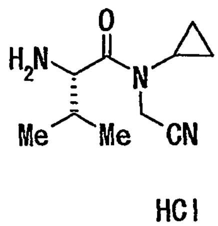
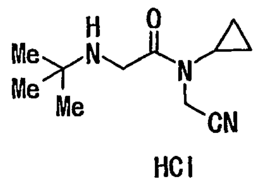
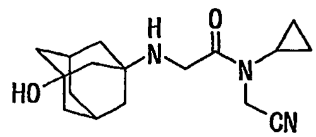
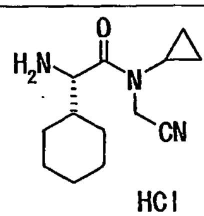
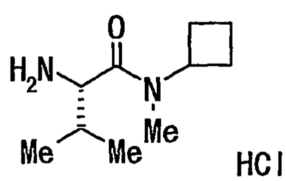
Example No.	Compound	NMR
Example 2		^{1}H-NMR(δppm, DMSO-d_6) 0.84-0.94(2H, m), 1.00-1.17 (7H, m), 1.19-1.30(1H, m), 2.03-2.20(1H, m), 2.90-2.95 (1H, m), 4.32(1H, d, J=13.2Hz), 4.30-4.35 (1H, m), 4.57(1H, d, J=13.2Hz), 8.61(3H, brs).
Example 3		^{1}H-NMR(δppm, DMSO-d_6) 0.95-1.00(4H, m), 1.30(9H, s), 2.96-3.03(1H, m), 4.07(2H, brs), 4.46(2H, s), 8.94(2H, brs).
Example 4		^{1}H-NMR(δppm, $CDCl_3$) 0.89-0.96 (2H, m), 1.03-1.06 (2H, m), 1.48-1.85(14H, m), 2.28(2H, brs), 2.48-2.83(1H, m), 3.64(2H, s), 4.29(2H, s).
Example 5		^{1}H-NMR(δppm, DMSO-d_6) 0.89-0.92 (2H, m), 1.06-1.23 (7H, m), 1.61-1.93(6H, m), 2.92-2.95(1H, m), 4.31(1H, d, J=8Hz), 4.37(1H, d, J=12Hz), 8.32(3H, brs).
Example 6		^{1}H-NMR(δppm, DMSO-d_6) 0.88-0.91(3H, m), 0.95-0.98 (3H, m), 1.55-1.67(2H, m), 1.90-2.32(5H, m), 2.88(1.5H, s), 2.98(1.5H, s), 4.08-4.18 (0.5H, m), 4.25-4.33(0.5H, m), 4.48-4.60(0.5H, m), 4.70-4.82 (0.5H, m), 8.19(3H, brs).

Table 1-2

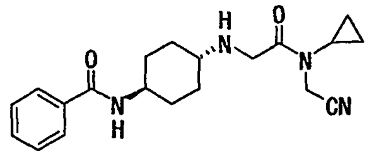
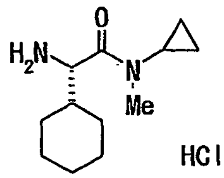
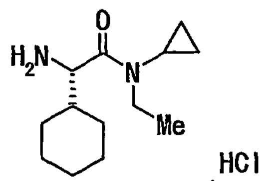
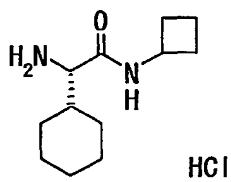
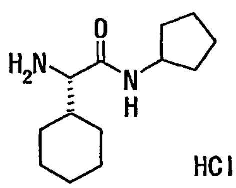
Example 7		^{1}H-NMR(δppm, $CDCl_3$) 0.81-0.90 (2H, m), 0.99-1.04 (2H, m), 1.20-1.40(3H, m), 1.90-2.04 (4H, m), 2.10-2.16 (2H, m), 2.46-2.50(1H, m), 2.78-2.83 (1H, m), 3.74(2H, s), 3.90-4.03 (1H, m), 4.23(2H, s), 5.93(1H, d, J=8.0Hz), 7.37-7.50(3H, m), 7.65-7.77(2H, m).
Example 8		^{1}H-NMR(δppm, DMSO-d_6) 0.75-0.85(2H, m), 0.90-1.22 (7H, m), 1.55-1.63(2H, m), 1.72-1.81(4H, m), 2.78-2.82 (1H, m), 2.87(3H, s), 4.26(1H, d, J=6.4Hz), 8.08(3H, brs).
Example 9		^{1}H-NMR(δppm, DMSO-d_6) 0.75-0.87(2H, m), 0.92-1.23 (10H, m), 1.58-1.62(2H, m), 1.65-1.85(4H, m), 2.73-2.80 (1H, m), 3.00-3.10(1H, m), 3.70-3.78(1H, m), 4.25(1H, d, J=6.4Hz), 8.18(3H, brs).
Example 10		^{1}H-NMR(δppm, DMSO-d_6) 0.96-1.21(5H, m), 1.55-1.73 (8H, m), 1.87-1.99(2H, m), 2.13-2.21(2H, m), 3.47(1H, d, J=6.3Hz), 4.17-4.25(1H, m), 8.17(3H, brs), 8.80(1H, d, J=4.2Hz).
Example 11		^{1}H-NMR(δppm, DMSO-d_6) 0.93-1.22(5H, m), 1.37-1.83 (14H, m), 3.49(1H, d, J=6.3Hz), 3.97-4.08(1H, m), 8.16(3H, brs), 8.45(1H, d, J=7.1Hz).

Table 1-3

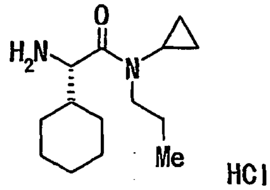
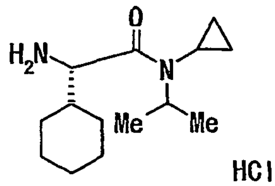
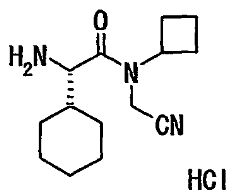
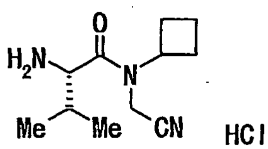
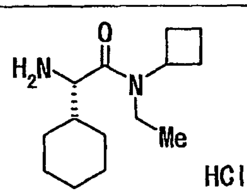
Example 12		^{1}H-NMR(δppm, DMSO-d_6) 0.75-0.90(5H, m), 1.97-1.30 (7H, m), 1.42-1.52(1H, m), 1.56-1.88(7H, m), 2.75-2.80 (1H, m), 2.83-2.95(1H, m), 3.68-3.77(1H, m), 4.30(1H, d, J=6.3Hz), 8.30(3H, brs).
Example 13		^{1}H-NMR(δppm, DMSO-d_6) 0.83-1.30(15H, m), 1.55-1.80 (6H, m), 2.60-2.70(1H, m), 4.08-4.18(1H, m), 4.30(1H, d, J=6.3Hz), 8.17(3H, brs).
Example 14		^{1}H-NMR(δppm, DMSO-d_6) 1.05-1.21(5H, m), 1.56-1.78 (8H, m), 2.05-2.20(2H, m), 2.25-2.37(2H, m), 4.30-4.40 (1H, m), 4.63(2H, s), 4.65-4.70(1H, m), 8.29(3H, brs).
Example 15		^{1}H-NMR(δppm, DMSO-d_6) 0.90(3H, d, J=6.9Hz), 0.97(3H, d, J=6.9Hz), 1.55-1.70(2H, m), 1.98-2.17(3H, m), 2.30-2.37 (2H, m), 4.41(1H, d, J=5.6Hz), 4.55(2H, s), 4.56-4.68(1H, m), 8.23(3H, brs).
Example 16		^{1}H-NMR(δppm, DMSO-d_6) 1.01-1.17(8H, m), 1.57-1.75 (8H, m), 2.00-2.25(4H, m), 3.30-3.50(2H, m), 3.92(0.35H, d, J=6.1Hz), 4.18(0.65H, d, J=5.6Hz), 4.36-4.47(1H, m), 8.09(3H, brs).

Table 1-4

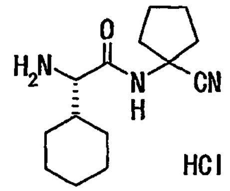
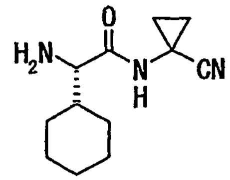
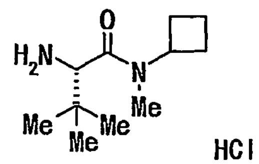
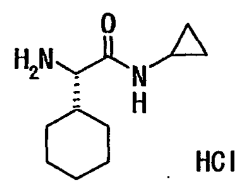
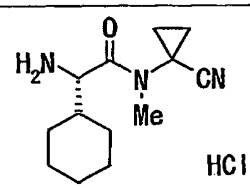
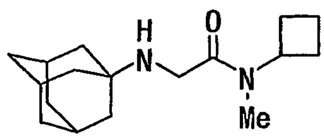
Example 17		^{1}H-NMR(δppm, DMSO-d_6) 0.98-1.23(5H, m), 1.55-1.80 (10H, m), 2.05-2.20(4H, m), 3.64(1H, d, J=6.0Hz), 8.30(3H, brs), 9.32(1H, s).
Example 18		^{1}H-NMR(δppm, $CDCl_3$) 0.95-1.80 (16H, m), 1.90-2.00 (1H, m), 3.23(1H, d, J=3.6Hz), 7.91(1H, s).
Example 19		^{1}H-NMR(δppm, DMSO-d_6) 0.96 (5.4H, s), 0.98(3.6H, s), 1.63-1.72(2H, m), 1.99-2.30 (4H, m), 2.88(1.7H, s), 3.01 (1.3H, s), 4.11(0.4H, s), 4.30 (0.6H, s), 4.70-4.75(1H, m), 8.05(3H, brs).
Example 20		^{1}H-NMR(δppm, DMSO-d_6) 0.38-0.55(2H, m), 0.61-0.70 (2H, m), 0.97-1.19(5H, m), 1.52-1.75(6H, m), 2.65-2.71 (1H, m), 3.43(1H, d, J=6.5Hz), 8.18(3H, brs), 8.63(1H, d, J=4.2Hz).
Example 21		^{1}H-NMR(δppm, DMSO-d_6) 0.98-1.25 (6H, m), 1.45-1.80 (9H, m), 2.97(0.6H, s), 3.11(2.4H, s), 4.12(1H, d, J=5.6Hz), 8.28(3H, brs).
Example 22		^{1}H-NMR(δppm, $CDCl_3$) 1.55-1.75 (8H, m), 1.86(1H, s), 2.04-2.30(6H, m), 2.88(1.5H, s), 2.93(1.5H, s), 3.37(1H, s), 3.42(1H, s), 4.18-4.29(0.5H, m), 4.89-5.00(0.5H, m).

Table 1-5

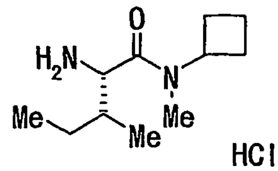
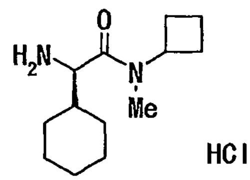
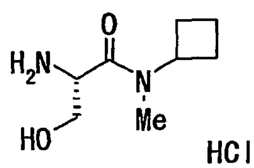
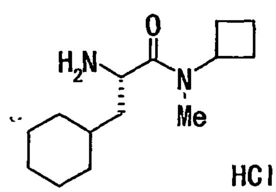
Example 23		^{1}H-NMR(δppm, DMSO-d_6) 0.82-0.87(3H, m), 0.91-0.94 (3H, m), 1.06-1.15(1H, m), 1.57-1.84(3H, m), 1.99-2.34 (3H, m), 2.88(1.8H, s), 2.98 (1.2H, s), 4.15(0.4H, d, J=5.3Hz), 4.30(0.6H, d, J=5.1Hz), 4.47-4.55(0.6H, m), 4.70-4.79(0.4H, m), 8.11(3H, brs).
Example 24		^{1}H-NMR(δppm, DMSO-d_6) 1.03-1.18(5H, m), 1.59-1.73 (8H, m), 1.99-2.28(4H, m), 2.88(1.7H, s), 2.98(1.3H, s), 4.10(0.4H, d, J=5.4Hz), 4.26 (0.6H, d, J=5.4Hz), 4.42-4.58 (0.6H, m), 4.69-4.80(0.4H, m), 8.12(3H, brs).
Example 25		^{1}H-NMR(δppm, DMSO-d_6) 1.58-1.66(2H, m), 2.00-2.30 (4H, m), 2.87(1.8H, s), 2.99(1.2H, s), 3.51-3.62(1H, m), 3.65-3.75(1H, m), 4.24-4.29(0.5H, m), 4.38-4.41 (0.5H, m), 4.47-4.56(0.5H, m), 4.74-4.82(0.5H, m), 5.52(1H, brs), 8.16(3H, brs).
Example 26		^{1}H-NMR(δppm, DMSO-d_6) 0.80-0.95(2H, m), 1.10-1.25 (4H, m), 1.40-1.67(8H, m), 1.82-1.87(1H, m), 1.95-2.20 (3H, m), 2.25-2.33(1H, m), 2.87(1.5H, s), 2.94(1.5H, s), 4.21-4.26(0.5H, m), 4.30-4.42 (1H, m), 4.71-7.83(0.5H, m), 8.15(3H, brs).

Table 1-6

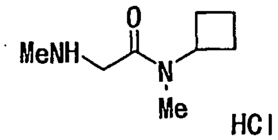
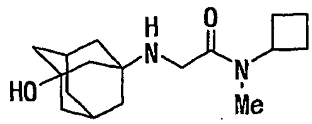
Example 27		^{1}H-NMR(δppm, DMSO-d_6) 1.55-1.68(2H, m), 1.96-2.05 (1H, m), 2.06-2.30(3H, m), 2.53(1.5H, s), 2.87(3H, s), 3.95(1H, s), 4.00(1H, s), 4.15-4.22(0.5H, m), 4.77-4.89 (0.5H, m), 8.92(3H, brs).
Example 28		^{1}H-NMR(δppm, $CDCl_3$) 1.51-1.77 (14H, m), 1.88(2H, brs), 2.05-2.30(6H, m), 2.88 (1.5H, s), 2.93(1.5H, s), 3.37 (1H, s), 3.42(1H, s), 4.15-4.25 (0.5H, m), 4.90-4.97 (0.5H, m).

Table 1-7

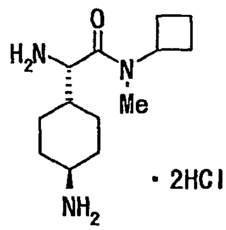
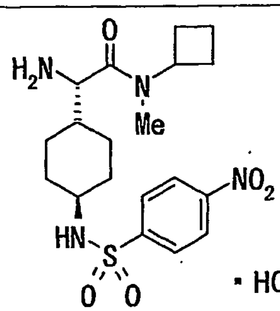
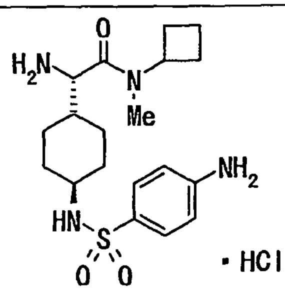
Example 30		^{1}H-NMR(δppm, DMSO-d_6) 1.11-1.40 (4H, m), 1.54-1.80 (5H, m), 1.93-2.35(6H, m), 2.78-2.91 (1H, m), 2.88(1.65H, s), 2.98 (1.35H, s), 4.13(0.45H, d, J=5.6Hz), 4.29(0.55H, d, J=5.8Hz), 4.47-4.58(0.55H, m), 4.68-4.79 (0.45H, m), 8.15(6H, bs).
Example 31		^{1}H-NMR(δppm, DMSO-d_6) 0.96-1.20 (4H, m), 1.35-1.77 (7H, m), 1.84-2.31(4H, m), 2.79-2.94 (4H, m), 4.01-4.07 (0.45H, d, J=4Hz), 4.15-4.21 (0.55H, d, J=4Hz), 4.38-4.51 (0.55H, m), 4.62-4.76 (0.45H, m), 7.90-8.15 (6H, m), 8.32-8.47(2H, d, J=8.8Hz).
Example 32		^{1}H-NMR(δppm, DMSO-d_6) 0.91-1.21 (4H, m), 1.32-1.71 (7H, m), 1.84-2.34(4H, m), 2.57-2.72 (1H, m), 2.79-2.95 (3H, s), 3.88-4.33 (3.28H, m), 4.61-4.77 (0.72H, m), 6.48-6.73 (2H, d, J=8.8Hz), 7.04-7.26(1H, m), 7.31-7.51(2H, d, J=8.8Hz), 7.87-8.14(3H, m).

Table 1-8

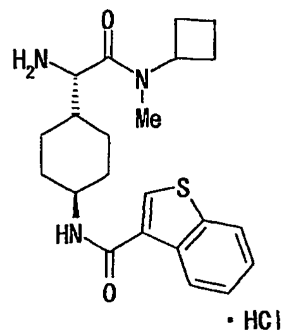
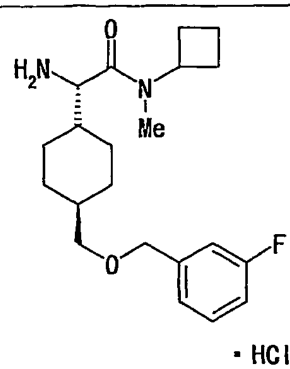
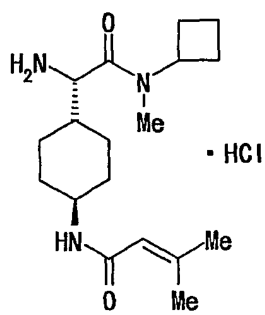
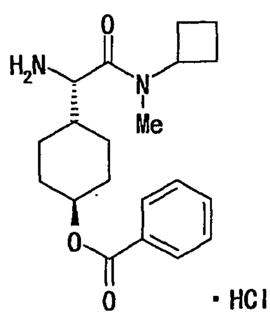
Example 35		^{1}H-NMR(δppm, DMSO-d_6) 1.16-1.46 (4H, m), 1.51-1.82(5H, m), 1.83-2.42(6H, m), 2.91 (1.75H, s), 3.02(1.25H, s), 3.62-3.85 (1H, m), 4.19(0.42H, d, J=5.3Hz), 4.34(0.58H, d, J=6.0Hz), 4.49-4.67(0.58H, m), 4.71-4.86(0.42H, m), 7.35-7.50 (2H, m), 7.97-8.06(1H, m), 8.14 (3H, brs), 8.25-8.47(3H, m).
Example 36		^{1}H-NMR(δppm, DMSO-d_6) 0.78-1.32 (4H, m), 1.39-1.86 (8H, m), 1.93-2.37(4H, m), 2.88(1.72H, s), 2.98(1.28H, s), 3.23(2H, d, J=6.3Hz), 4.13(0.42H, d, J=5.1Hz), 4.28(0.58H, d, J=5.4Hz), 4.45(2H, s), 4.47-4.60(0.58H, m), 4.69-4.83 (0.42H, m), 7.03-7.21(3H, m), 7.32-7.44(1H, m), 8.06(3H, brs).
Example 37		^{1}H-NMR(δppm, DMSO-d_6) 1.00-1.30 (4H, m), 1.55-1.65(5H, m), 1.75 (3H, s), 1.75-1.81(2H, m), 1.95-2.35(4H, m), 2.05(3H, s), 3.38-3.43(1H, m), 4.12-4.16 (0.4H, m), 4.21-4.25(0.6H, m), 4.52-4.56(0.6H, m), 4.73-4.77 (0.4H, m), 5.58(1H, d, J=4.8Hz), 7.62(1H, d, J=8Hz), 8.14(3H, brs).
Example 38		^{1}H-NMR(δppm, DMSO-d_6) 1.25-1.55 (4H, m), 1.60-1.85(5H, m), 1.97-2.35(6H, m), 2.91 (1.74H, s), 3.01(1.26H, s), 4.21(0.42H, d, J=6.0Hz), 4.35 (0.58H, d, J=6.0Hz), 4.56 (0.58H, m), 4.78(1.42H, m), 7.51(2H, dd, J=8.4Hz, 7.2Hz), 7.65(2H, t, J=7.2Hz), 7.93(2H, d, J=8.4Hz), 8.01(3H, brs).

Table 1-9

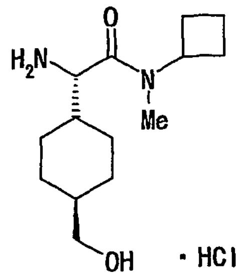
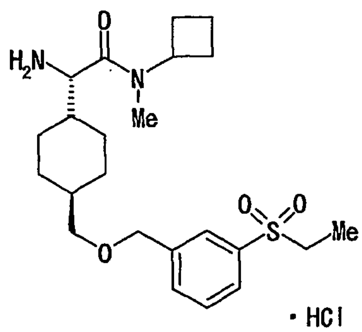
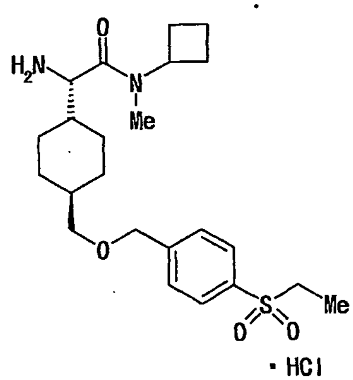
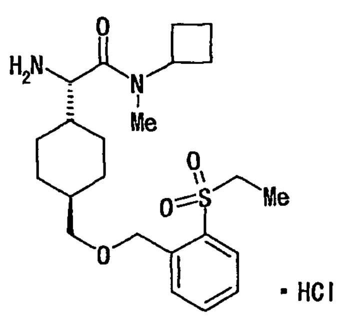
Example 39		^{1}H-NMR(δppm, DMSO-d_6) 0.75-0.95(2H, m), 1.00-1.40(3H, m), 1.55-1.80(7H, m), 1.95-2.35 (4H, m), 2.88(1.74H, s), 2.97 (1.26H, s), 3.18(2H, t-like), 4.13(0.42H, d, J=5.2Hz), 4.27 (0.58H, d, J=5.2Hz), 4.39(1H, t, J=4.8Hz), 4.53(0.58H, m), 4.77 (0.42H, m) 8.03(3H, brs).
Example 40		^{1}H-NMR(δppm, DMSO-d_6) 0.85-1.00 (2H, m), 1.07(3H, t, J=7.2Hz), 1.10-1.20(2H, m), 1.35-1.80(8H, m), 1.90-2.30(4H, m), 2.86 (1.74H, s), 2.95(1.26H, s), 3.26 (4H, m), 4.10(0.42H, d, J=5.6Hz), 4.25(0.58H, d, J=5.6Hz), 4.53 (2H, s), 4.45-4.55(0.58H, m), 4.75 (0.42H, m), 7.63(2H, m), 7.77 (2H, m), 7.83(3H, brs).
Example 41		^{1}H-NMR(δppm, DMSO-d_6) 0.85-1.00 (2H, m), 1.06(3H, t, J=7.2Hz), 1.10-1.25(2H, m), 1.45-1.85(8H, m), 1.90-2.35(4H, m), 2.86 (1.74H, s), 2.95(1.26H, s), 3.25 (4H, m), 4.11(0.42H, d, J=5.6Hz), 4.26(0.58H, d, J=5.6Hz), 4.54 (2H, s), 4.45-4.60 (0.58H, m), 4.74 (0.42H, m), 7.54(2H, d, J=8.0Hz), 7.82(2H, d, J=8.0Hz), 8.00(3H, brs).
Example 42		^{1}H-NMR(δppm, DMSO-d_6) 0.85-1.00 (2H, m), 1.09(3H, t, J=7.2Hz), 1.10-1.25(2H, m), 1.45-1.85(8H, m), 1.95-2.35(4H, m), 2.88 (1.74H, s), 2.98(1.26H, s), 3.33 (4H, m), 4.13(0.42H, d, J=5.6Hz), 4.28(0.58H, d, J=5.6Hz), 4.52 (0.58H, m), 4.75 (0.42H, m), 4.82 (2H, s), 7.55-7.76(3H, m), 7.89 (1H, d, J=7.6Hz), 8.03(3H, brs).

Table 1-10

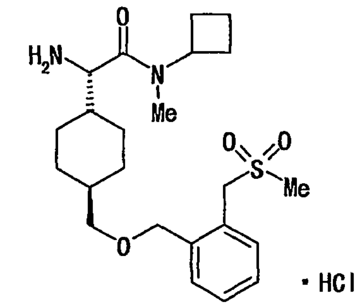
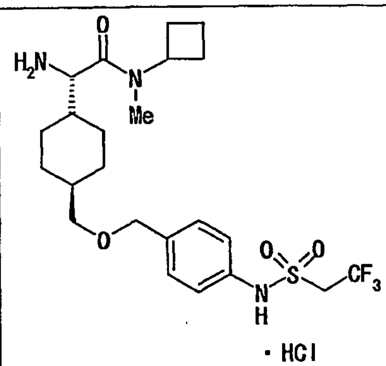
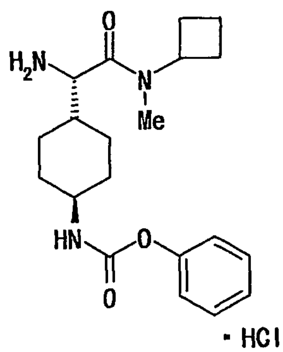
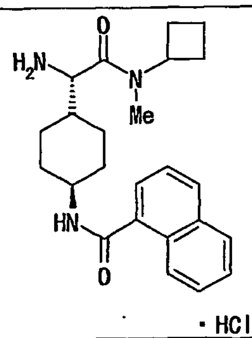
Example 43		^{1}H-NMR(δppm, DMSO-d_6) 0.80-1.00 (2H, m), 1.05-1.25(2H, m), 1.40-1.80(8H, m), 1.95-2.35 (4H, m), 2.88(1.74H, s), 2.97 (3H, s), 2.98(1.26H, s), 3.24 (2H, d, J=6.4Hz), 4.13 (0.42H, d, J=5.6Hz), 4.28 (0.58H, d, J=5.6Hz), 4.56(2H, s), 4.59(2H, s), 4.45-4.60 (0.58H, m), 4.76 (0.42H, m), 7.31-7.41(4H, m), 8.01(3H, brs).
Example 44		^{1}H-NMR(δppm, DMSO-d_6) 0.80-1.00 (2H, m), 1.00-1.25(2H, m), 1.46 (1H, m), 1.63(4H, m), 1.78(2H, m), 1.95-2.35(4H, m), 2.88(1.74H, s), 2.97(1.26H, s), 3.21(2H, d, J=6.4Hz), 4.14 (0.42H, brs), 4.30(0.58H, brs), 4.38(2H, s), 4.49(2H, q, J=9.6Hz), 4.76(0.42H, m), 7.18 (2H, d, J=8.8Hz), 7.27 (2H, d, J=8.8Hz), 8.04(3H, brs), 10.43 (1H, brs).
Example 45		^{1}H-NMR(δppm, DMSO-d_6) 1.05-1.35 (4H, m), 1.53-1.75(5H, m), 1.84 - 2.38(6H, m), 2.90 (1.74H, s), 2.99(1.26H, s), 3.16 -3.33(1H, m), 4.15(0.42H, d, J=5.1Hz), 4.29(0.58H, d, J=5.5Hz), 4.46 - 4.62(0.58H, m), 4.69-4.83 (0.42H, m), 7.07(2H, d, J=7.7Hz), 7.19(1H, dd, J=7.4Hz, 7.1Hz), 7.37(2H, dd, J=7.7, 7.3Hz), 7.63 -7.74(1H, m), 7.78-8.56(3H, brs).
Example 46		^{1}H-NMR(δppm, DMSO-d_6) 1.20-1.44 (4H, m), 1.56-1.78(5H, m), 1.92 - 2.36(6H, m), 2.91(1.74H, s), 3.01(1.26H, s), 3.70-3.83(1H, m), 4.15-4.23 (0.42H, m), 4.29-4.38 (0.58H, m), 4.51-4.62 (0.58H, m), 4.71-4.83(0.42H, m), 7.48-7.58 (4H, m), 7.92-8.02(2H, m), 8.06 - 8.20(4H, m), 8.36-8.44 (1H, m).

Table 1-11

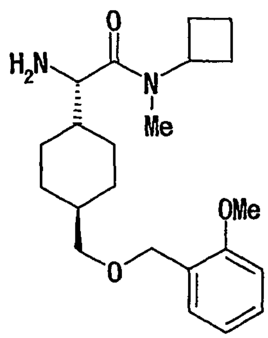
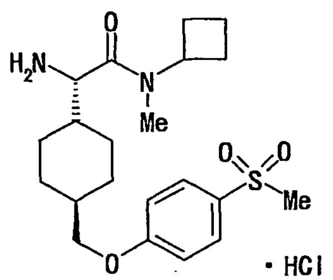
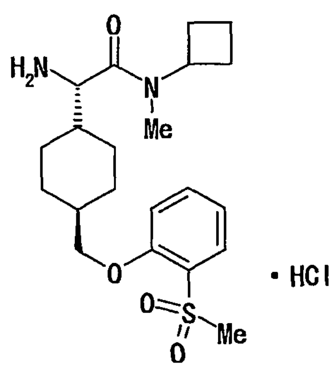
Example 47		^{1}H-NMR(δppm, $CDCl_3$) 0.86-1.29 (4H, m), 1.35-1.78(7H, m), 1.79 -1.95(3H, m), 2.00-2.35 (4H, m), 2.94(1.74H, s), 2.95 (1.26H, s), 3.30(2H, d, J=6.5Hz), 3.43 (0.42H, d, J=5.8Hz), 3.53 (0.58H, d, J=6.1Hz), 3.81(3H, s), 4.32-4.43(0.58H, m), 4.52 (2H, s), 4.86-4.97(0.42H, m), 6.83(1H, d, J=8.1Hz), 6.93(1H, dd, J=7.5Hz, 7.5Hz), 7.23(1H, dd, J=8.1Hz, 7.5Hz), 7.35(1H, d, J=7.4Hz).
Example 48		^{1}H-NMR(δppm, DMSO-d_6) 0.93-1.33 (4H, m), 1.55-1.77(6H, m), 1.82 -2.36(6H, m), 2.89 (1.74H, s), 2.99(1.26H, s), 3.14(3H, s), 3.88(2H, d, J=6.3Hz), 4.16 (0.42H, d, J=5.3Hz), 4.30 (0.58H, d, J=5.5Hz), 4.49-4.60 (0.58H, m), 4.71-4.83(0.42H, m), 7.13(2H, d, J=8.8Hz), 7.81 (2H, d, J=8.8Hz), 7.91-8.25(3H, brs).
Example 49		^{1}H-NMR(δppm, DMSO-d_6) 1.01-1.31 (4H, m), 1.55-1.80(6H, m), 1.86-2.37(6H, m), 2.90 (1.74H, s), 3.00(1.26H, s), 3.23(3H, s), 3.93-4.03(2H, m), 4.16(0.42H, d, J=5.8Hz), 4.32 (0.58H, d, J=5.1Hz), 4.50-4.61 (0.58H, m), 4.72-4.84(0.42H, m), 7.13(1H, dd, J=7.5Hz, 7.4Hz), 7.25(1H, d, J=8.6Hz), 7.66(1H, dd, J=7.9Hz, 8.2Hz), 7.78(1H, d, J=7.7Hz), 8.00-8.21(3H, brs).

Table 1-12

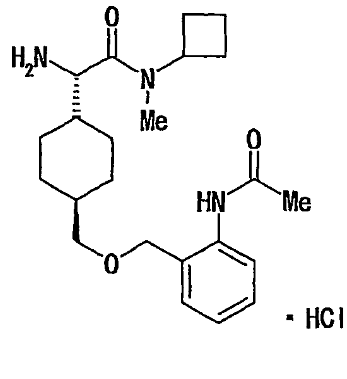
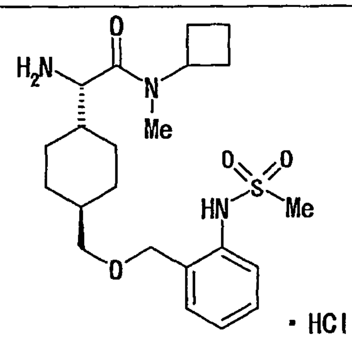
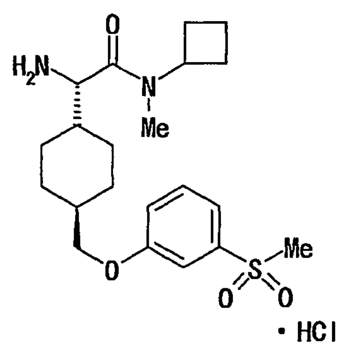
Example 50		^{1}H-NMR(δppm, DMSO-d_6) 0.79-1.29 (4H, m), 1.40-1.86(8H, m), 1.93-2.37(4H, m), 2.04(3H, s), 2.88(1.74H, s), 2.97(1.26H, s), 3.22(2H, d, J=5.5Hz), 4.09-4.19 (0.42H, m), 4.24-4.34 (0.58H, m), 4.43(2H, s). 4.48-4.58 (0.58H, m), 4.70-4.83 (0.42H, m), 7.13(1H, dd, J=7.4, 7.0Hz), 7.24(1H, dd, J=8.1Hz, 7.7Hz), 7.34(1H, d, J=7.8Hz), 7.46(1H, d, J=7.7Hz), 7.94-8.18 (3H, brs), 9.28(1H, s).
Example 51		^{1}H-NMR(δppm, DMSO-d_6) 0.80-1.31 (4H, m), 1.42-1.85(8H, m), 1.93-2.36(4H, m), 2.88 (1.74H, s), 2.98(4.26H, s), 3.25(2H, d, J=6.2Hz), 4.10-4.19 (0.42H, m), 4.25-4.34(0.58H, m), 4.46-4.62 (0.58H, m), 4.56 (2H, s), 4.70-4.83(0.42H, m), 7.20-7.36 (3H, m), 7.40(1H, d, J=7.5Hz), 7.94-8.17(3H, brs), 8.94(1H, s).
Example 52		^{1}H-NMR(δppm, DMSO-d_6) 0.94-1.33 (4H, m), 1.56-1.81(6H, m), 1.83-2.36(6H, m), 2.89(1.74H, s), 2.99(1.26H, s), 3.21(3H, s), 3.87(2H, d, J=6.2Hz), 4.16 (0.42H, d, J=5.6Hz), 4.31 (0.58H, d, J=5.3Hz), 4.48-4.61 (0.58H, m), 4.71-4.84(0.42H, m), 7.26(1H, d, J=7.9Hz), 7.38 (1H, d, J=1.9Hz), 7.47(1H, d, J=7.7Hz), 7.54(1H, dd, J=7.9Hz, 7.9Hz), 7.96-8.24(3H, brs).

Table 1-13

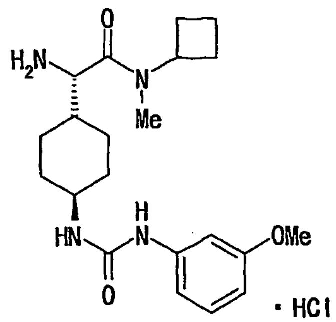
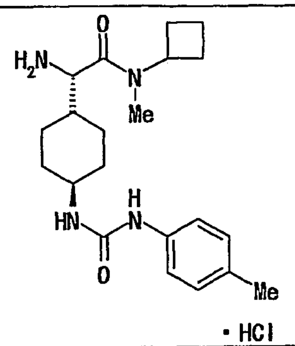
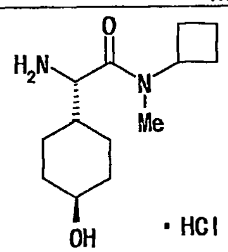
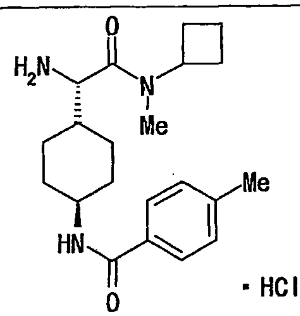
Example 53		^{1}H-NMR(δppm, DMSO-d_6) 0.91-1.38 (4H, m), 1.46-1.76(5H, m), 1.79-2.38(6H, m), 2.83-3.00(3H, s), 3.68(3H, s),3.22-3.40(1H, m), 4.08-4.21(0.4H, m), 4.29-4.36(0.6H, m), 4.44-4.61 (0.6H, m), 4.66-4.83(0.4H, m), 6.19(1H, d, J=8Hz), 6.41(1H, m), 6.78(1H, d, J=8Hz), 6.96-7.15 (2H, m), 7.90-8.21(3H, br), 8.55(1H, s).
Example 54		^{1}H-NMR(δppm, DMSO-d_6) 0.87-1.39 (4H, m), 1.49-1.77(5H, m), 1.81-2.37(9H, m), 2.83-3.02(1H, s), 3.19-3.42(1H, m), 4.08-4.21 (0.4H, m), 4.23-4.36(0.6H, m), 4.45-4.59(0.6H, m), 4.68-4.81 (0.4H, m), 6.11(1H, d, J=8Hz), 6.97(2H, d, J=8Hz), 7.20(2H, d, J=8Hz), 7.91-8.18(3H, br), 8.38(1H, s).
Example 55		^{1}H-NMR(δppm, DMSO-d_6) 0.86-1.42 (4H, m), 1.48-2.38(11H, m), 2.76-3.04(3H, s), 2.12-3.30(1H, m), 4.05-4.15(0.4H, d, J=4Hz), 4.19-4.31(0.6H, d, J=4Hz), 4.40-4.59(1.6H, m), 4.67-4.80 (0.4H, m), 7.84-8.20(3H, br).
Example 56		^{1}H-NMR(δppm, DMSO-d_6) 1.11-1.42 (4H, m), 1.49-1.76(5H, m), 1.76-1.92(9H, m), 2.82-3.06(3H, s), 3.56-3.77(1H, m), 4.09-4.20 (0.4H, d, J=4Hz), 4.25-4.36 (0.6H, d, J=4Hz), 4.47-4.64 (0.6H, m), 4.67-4.84(0.4H, m), 7.21(2H, d, J=8Hz), 7.70(2H, d, J=8Hz), 7.93-8.25(4H, br).

Table 1-14

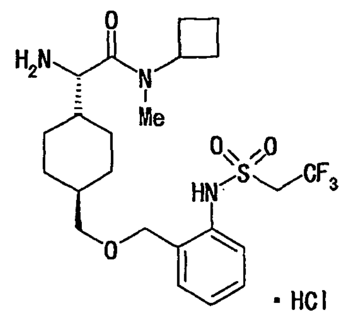
Example 57		^{1}H-NMR(δppm, DMSO-d_6) 0.84-1.18 (4H, m), 1.41-1.84(7H, m), 1.99-2.32(4H, m), 2.89 (1.68H, s), 2.98(1.32H, s), 3.27(2H, d, J=6.78Hz), 4.16(0.44H, m), 4.32(0.56H, m), 4.52(2H, d, J=9.42Hz), 4.56(2H, s), 4.46-4.60(0.44H, m), 4.78(0.56H, m), 7.30-7.45(4H, m), 8.02(3H, brs), 9.68(1H, s).

Table 1-15

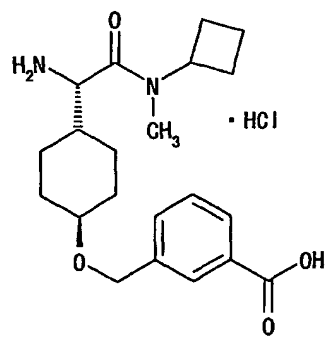
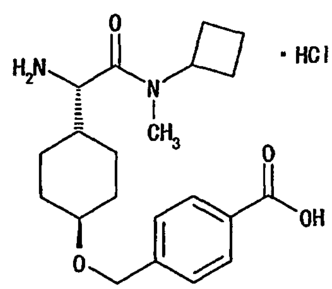
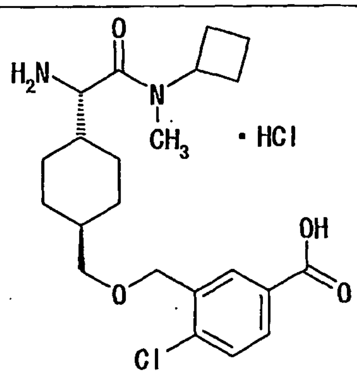
Example 58		^{1}H-NMR(δppm, DMSO-d_6) 1.09-1.19 (4H, m), 1.54-2.33 (12H, m), 2.88 (1.60H, s), 2.97 (1.40H, s), 4.09-4.19 (0.46H, m), 4.25-4.34 (0.64H, m), 4.46-4.56 (0.50H, m), 4.56 (2H, s), 4.70-4.80 (0.50H, m), 7.46 (1H, t, J=7.7Hz), 7.54 (1H, d, J=7.9Hz), 7.83 (1H, d, J=7.4Hz), 7.88 (1H, s), 8.05 (3H, s).
Example 59		^{1}H-NMR(δppm, DMSO-d_6) 1.09-1.18 (4H, m), 1.54-2.31 (12H, m), 2.87 (1.79H, s), 2.96 (1.21H, s), 3.28 (2H, s), 4.09-4.18 (0.40H, m), 4.25-4.32 (0.60H, m), 4.45-4.56 (0.56H, m), 4.57 (2H, s), 4.70-4.81 (0.44H, m), 7.41 (2H, d, J=8.3Hz), 7.90 (2H, d, J=8.3Hz), 7.99 (3H, brs).
Example 60		^{1}H-NMR(δppm, DMSO-d_6) 0.99-1.10 (4H, m), 1.69-2.12 (12H, m), 2.88 (1.83H, s), 2.96 (1.17H, s), 3.31 (2H, s), 4.07-4.20 (0.49H, m), 4.24-4.34 (0.51H, m), 4.49-4.62 (2.55H, m), 4.68-4.82 (0.45H,m), 7.55-7.58 (1H, m), 7.83-7.86 (1H, m), 8.01-8.03 (4H, m).

Table 1-16

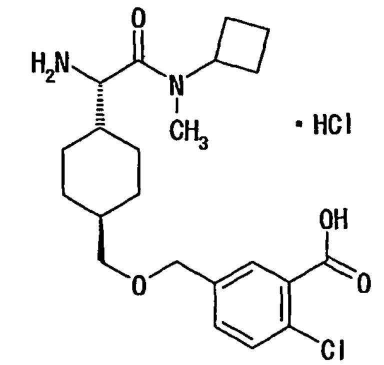
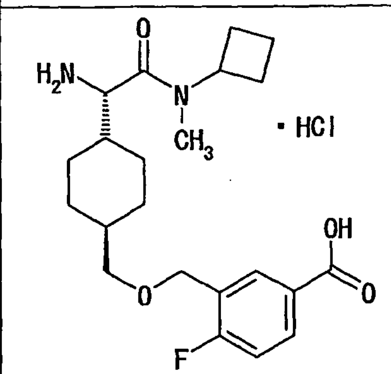
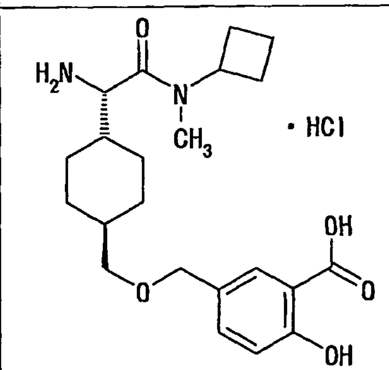
Example 61		^{1}H-NMR(δppm, DMSO-d_6) 0.85-1.20 (4H, m), 1.46-2.29 (12H, m), 2.87 (1.85H, s), 2.94 (1.15H, s), 3.22 (2H, d, J=6.0Hz), 4.07-4.17 (0.49H, m), 4.22-4.31 (0.51H, m), 4.44-4.54 (2.58H, m), 4.70-4.80 (0.42H, m), 7.41-7.45 (1H, m), 7.48-7.52 (1H, m), 7.68-7.72 (1H, m), 8.05 (3H, brs).
Example 62		^{1}H-NMR(δppm, DMSO-d_6) 0.82-1.27 (4H, m), 1.47-2.30 (12H, m), 2.84 (1.86H, s), 2.94 (1.14H, s), 3.27 (2H, d, J=8.1Hz), 4.08-4.22 (0.47H, m), 4.21-4.31 (0.53H, m), 4.45-4.58 (2.53H, m), 4.66-4.79 (0.47H, m), 7.27-7.32 (1H, m), 7.87-7.92 (1H, m), 7.98-8.01 (1H, m), 8.10 (3H, brs).
Example 63		^{1}H-NMR(δppm, DMSO-d_6) 0.99-1.13 (4H, m), 1.36-2.31 (12H, m), 2.88 (1.79H, s), 2.97 (1.21H, s), 3.17-3.21 (2H, m), 4.08-4.18 (0.50H, m), 4.23-4.33 (0.50H, m), 4.35 (2H, s), 4.49-4.60 (0.44H, m), 4.70-4.81 (0.56H, m), 6.93-6.98 (1H, m), 7.42-7.47 (1H, m), 7.70-7.74 (1H, m), 8.12 (3H, brs).

Table 1-17

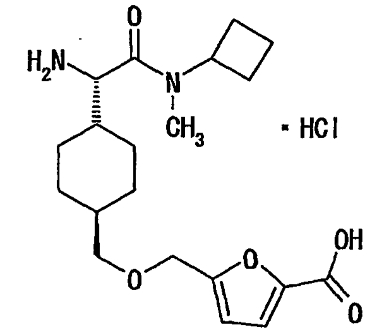
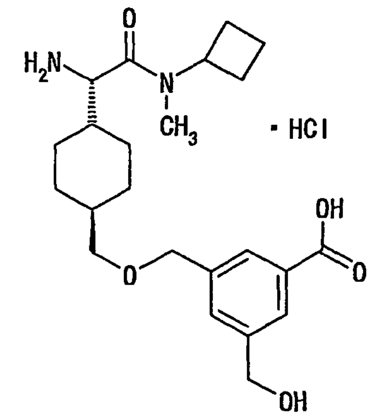
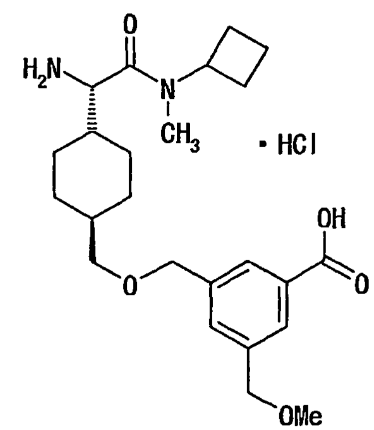
Example 64		^{1}H-NMR(δppm, DMSO-d_6) 0.81-1.22 (4H, m), 1.34-2.28 (12H, m), 2.87 (1.83H, s), 2.96 (1.17H, s), 3.22 (2H, d, J=6.0Hz), 4.12-4.16 (0.43H, m), 4.21-4.31 (0.57H, m), 4.41 (2H, s), 4.46-4.56 (0.55H, m), 4.68-4.79 (0.45H, m), 6.56 (1H, d, J=3.2Hz), 7.14 (1H, d, J=3.2Hz), 8.10 (3H, brs).
Example 65		^{1}H-NMR(δppm, DMSO-d_6) 0.91-1.23(4H, m), 1.75-2.02 (12H, m), 2.89 (1.7H, s), 2.98 (1.3H, s), 3.25 (2H, d, J=6.0Hz), 4.09-4.19 (0.37H, m), 4.23-4.33 (0.63H, m), 4.45-4.56 (4.6H, m), 4.70-4.80 (0.4H, m), 7.48 (1H, s), 7.74 (1H, s), 7.82 (1H, s), 8.08(3H, brs).
Example 66		^{1}H-NMR(δppm, DMSO-d_6) 0.86-1.22 (4H, m), 1.48-2.32 (12H, m), 2.88 (1.66H, s), 2.95 (1.34H, s), 3.24 (2H, d, J=5.3Hz), 3.30 (3H, s), 4.08-4.17 (0.39H, m), 4.22-4.31 (0.61H, m), 4.40-4.57 (4.52H, m), 4.68-4.79 (0.48H, m), 7.45-7.49 (1H, m), 7.73-7.83 (2H, m), 8.07 (3H, brs).

Table 1-18

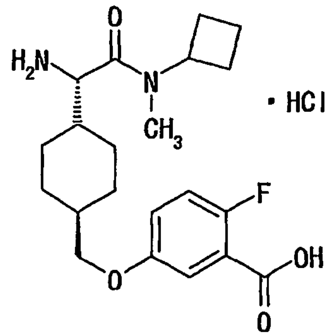
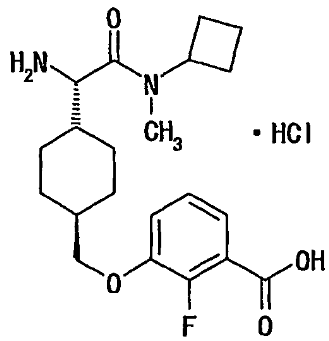
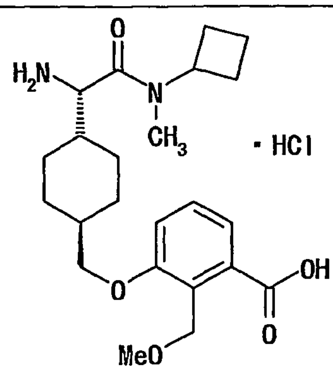
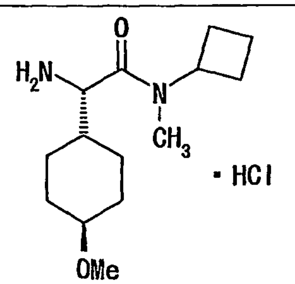
Example 67		^{1}H-NMR(δppm, DMSO-d_6) 1.00-1.22(4H, m), 1.63-2.31 (16H, m), 2.89(1.80H, s), 2.98(1.20H, s), 4.16(0.40H, d, J=4.6Hz), 4.30(0.60H, d, J=4.6Hz), 4.48-4.58(0.48H, m), 4.71-4.82(0.52H, m), 7.15-7.25 (3H, m), 8.00(3H, brs).
Example 68		^{1}H-NMR(δppm, DMSO-d_6) 1.05-1.18 (4H, m), 1.56-2.31 (12H, m), 2.88 (1.60H, s), 2.98 (1.40H, s), 3.15 (2H, d, J=4.6Hz), 3.86 (2H, d, J=6.0Hz), 4.15 (0.41H, d, J=5.6Hz), 4.30 (0.59H, d, J=5.6Hz), 4.48-4.58 (0.53H, m), 4.70-4.80 (0.47H, m), 7.13-7.19 (1H, m), 7.32-7.36 (2H, m), 8.06 (3H, brs).
Example 69		^{1}H-NMR(δppm, DMSO-d_6) 1.11-1.19 (4H,.m) 1.65-2.33 (12H, m), 2.90 (1.9H, s), 3.00 (1.1H, s), 3.19 (3H, s), 3.77-3.87 (2H, m), 4.13-4.21 (0.5H, m), 4.26-4.35 (0.5H, m), 4.50-4.60 (0.74H, m), 4.68 (2H, s), 4.73-4.83 (0.26H, m), 7.11-7.16 (1H, m), 7.20-7.24 (1H, m), 7.31-7.36 (1H, m), 8.12 (3H, brs).
Example 70		^{1}H-NMR(δppm, DMSO-d_6) 1.09-1.51(7H, m), 1.53-2.38(8H,m), 2.86(1.72H, s), 2.99(1.28H, s), 3.17(3H, s), 3.38(1H, m), 4.11(0.43H, m), 4.26(0.57H, m), 4.77(0.43H, m), 8.12(3H, brs).

Table 1-19

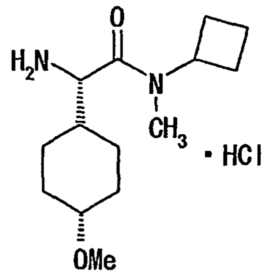
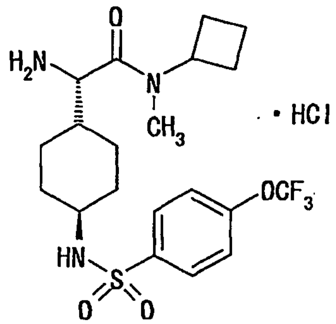
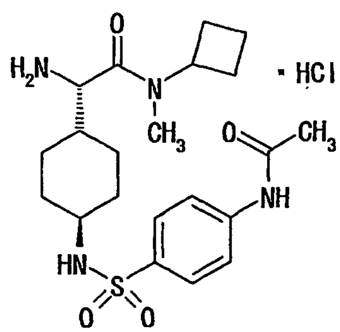
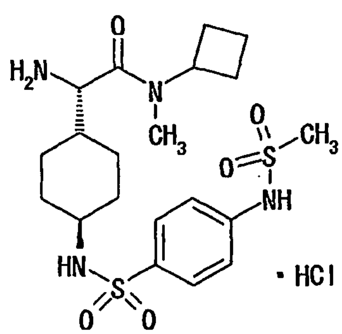
Example 71		^{1}H-NMR(δppm, DMSO-d_6) 0.88-1.32(4H, m), 1.50-1.76(5H, m), 1.92-2.34(6H, m), 2.89(1.49H,s), 2.97(1.51H, s), 3.16(3H, s), 3.31(1H, s), 4.14(0.44H, d, J=5.6Hz), 4.29(0.56H, d, J=5.6Hz), 4.56(0.56H, m), 4.76(0.44H, m), 8.02(3H, brs).
Example 72		^{1}H-NMR(δppm, DMSO-d_6) 0.92-1.27(4H, m), 1.38-1.76(7H, m), 1.89-2.38(4H, m), 2.78-2.90(2.72H, m), 2.91-2.96(1.27H, s), 4.06(0.43H, d, J=5.6Hz), 4.20(0.57H, d, J=0.56Hz), 4.47(0.43H, m), 4.72(0.43H, m), 7.55-7.63(2H, m), 7.84-7.96(3H, m), 8.05(3H, brs).
Example 73		^{1}H-NMR(DMSO-d_6) 0.95-1.22(4H, m), 1.39-1.74(7H, m), 1.88-2.36(7H, m), 2.75(1H, m), 2.94(1.31H, s), 2.85(1.69H, s), 4.05(0.44H, d, J=5.6Hz), 4.20(0.56H, d, J=5.6Hz), 4.45(0.56H, d, J=5.6Hz), 4.72(0.44H, m), 7.53(1H, m), 7.70(2H, d, J=8.8Hz), 7.76(2H, d, J=8.8Hz), 7.98(3H, brs), 10.41(1H, s).
Example 74		^{1}H-NMR(δppm, DMSO-d_6) 0.95-1.20(4H, m), 1.38(7H, m), 1.92(4H, m), 2.76(1H, m), 2.86(1.73H, s), 2.93(1.27H, s), 3.12(3H, s), 4.07(0.42H, d, J=5.1Hz), 4.21(0.58H, d, J=5.1Hz), 4.46(0.58H, m), 4.72(0.42H, m), 7.55-7.64(1H, m), 7.32(2H, d, J=8.8Hz), 7.73(2H, d, J=8.8Hz), 8.00(3H, brs).

Table 1-20

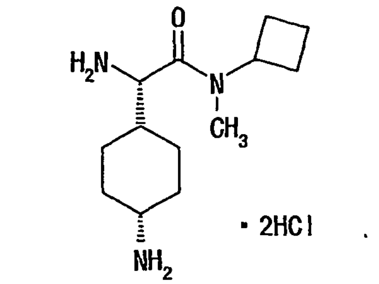
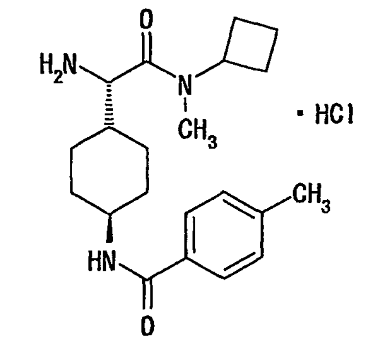
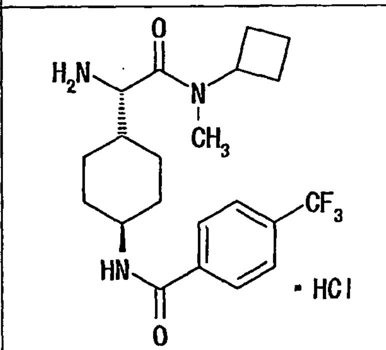
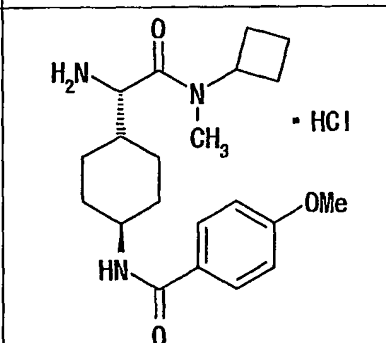
Example 75		^{1}H-NMR(δppm, DMSO-d_6) 1.32-2.39(15H, m), 2.89(1.81H, s), 3.02(1.19H, s), 3.31(1H, m), 4.10(0.39H, m), 4.26(0.61H, m), 4.77(0.39H, m), 8.23(6H, brs).
Example 76		^{1}H-NMR(δppm, DMSO-d_6) 1.15-1.42(4H, m), 1.53-1.78(5H, m), 1.78-1.94(2H, m), 1.94-2.40(7H, m), 2.90(1.81H, s), 3.01(1.19H, s), 3.69(1H, m), 4.17(0.41H, d, J=5.6Hz), 4.32(0.59H, d, J=5.6Hz), 4.57(0.59H, m), 4.77(0.41H, m),7.24(2H, d, J=8.3Hz), 7.73(2H, d, J=8.3Hz), 8.12(4H, brs).
Example 77		^{1}H-NMR(δppm, DMSO-d_6) 1.13-1.43(4H, m), 1.50-1.79(5H, m), 1.81-2.41(6H, m), 2.90(1.81H, s), 3.00(1.19H, s), 3.70H(1H, m), 4.16H(0.40H, d, J=5.6Hz), 4.32(0.60H, d, J=5.6Hz), 4.57(0.60H, m), 4.77(0.40H, m), 7.83(2H, d, 8.8Hz), 7.95-8.29(5H, brs), 8.53(1H, m).
Example 78		^{1}H-NMR(δppm, DMSO-d_6) 1.13-1.45(4H, m), 1.51-1.78(6H, m), 1.79-2.40(6H, m), 2.91(1.80H, m), 3.00(1.20H, s), 3.67(1H, m), 3.79(3H, s), 4.18(0.40H, brs), 4.33(0.60H, brs), 4.57(0.60H, m), (4.78H, m), 6.97(2H, d, J=9.3Hz), 7.80(2H, d, J=9.3Hz), 8.11(4H, brs).

Table 1—21

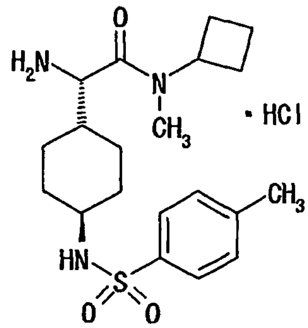
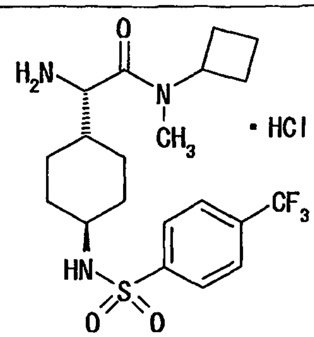
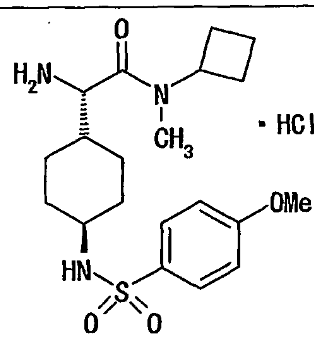
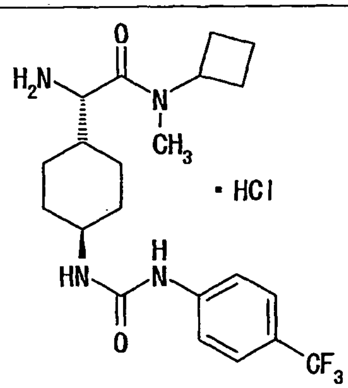
Example 79		^{1}H-NMR(δppm, DMSO-d_6) 0.94-1.20(4H, m), 1.40-1.72(7H, m), 1.72-2.43(7H, m), 2.76(1H, s), 2.85(1.68H, s), 2.93(1.32H, s), 4.05(0.44H, d, J=5.6Hz), 4.19(0.56H, d, J=5.6Hz), 4.46(0.56H, m), 4.72(0.44H, m), 7.38(2H, d, J=8.3), 7.61(1H, m), 7.68(2H, d, J=8.3Hz), 7.95(3H, brs).
Example 80		^{1}H-NMR(δppm, DMSO-d_6) 0.90-1.31(4H, m), 1.38-1.79(7H, m), 1.87-2.40(4H, m), 2.73-3.06 (4H, m), 4.06(0.44H, d, J=5.6Hz), 4.21(0.56d, J=5.6Hz), 4.46(0.56H, m), 4.72(0.44H, m), 7.84-8.12(4H, brs).
Example 81		^{1}H-NMR(δppm, DMSO-d_6) 0.92-1.27(4H, m), 1.39-1.74(7H, m), 1.92-2.38(4H, m), 2.75(1H, m), 2.85(1.76H, s), 2.94(1.24H, s), 3.83(3H, s), 4.04(0.42H, d, J=5.1Hz), 4.19(0.58H, d, J=5.1Hz), 4.47(0.58H, m), 4.73(0.42H, m), 7.10(2H, d, J=8.8Hz), 7.52(1H, m), 7.72(2H, d, J=8.8Hz), 7.86(3H, brs).
Example 82		^{1}H-NMR(δppm, DMSO-d_6) 0.94-1.43(4H, m), 1.51-1.80(5H, m), 1.81-2.39(6H, m), 2.89(1.70H, s), 3.00(1.30H, s), 3.36(1H, m), 4.18(0.43H, m), 4.32(0.57H, m), 4.54(0.57H, m), 4.77(0.43H, m), 6.42(1H, d, J=7.9Hz), 7.55(1H, m), 8.07(3H, brs), 9.09(1H, s).

Table 1—22

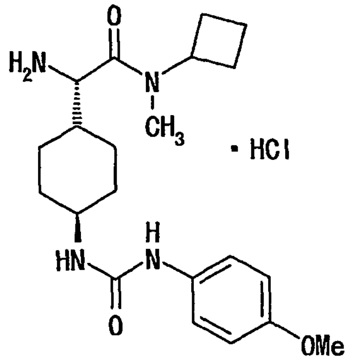
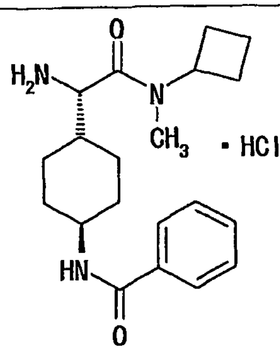
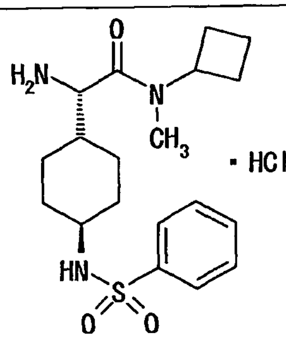
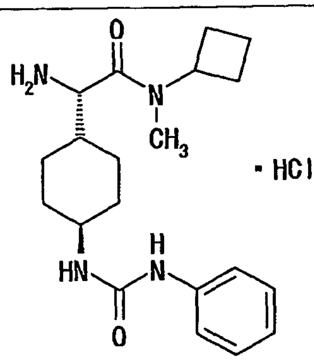
Example 83		^{1}H-NMR(δppm, DMSO-d_6) 0.95-1.42(4H, m), 1.50-1.79(5H, m), 1.81-2.41(6H, m), 2.90(1.73H, s), 3.00(1.27H, s), 3.36(1H, m), 3.67(3H, s), 4.17(0.42H, m), 4.32(0.58H, m), 4.54(0.58H, m), 4.77(0.42H, m), 6.06(1H, d, J=7.9Hz), 6.79(2H, m), 7.25(2H, m), 8.08(3H, brs), 8.31(1H, s).
Example 84		^{1}H-NMR(δppm, DMSO-d_6) 1.34-1.71 (8H, m), 1.72-1.95(3H, m), 1.95-2.41(4H, m), 2.91(1.65H, s), 3.03(1.39H, s), 4.06(1H, m), 4.14(0.46H, d, J=6.5Hz), 4.30(0.54H, d, J=6.5Hz), 4.55(0.54H, m), 4.78(0.46H, m), 7.40-7.56(3H, m), 7.85(3H, m), 8.15(3H, brs).
Example 85		^{1}H-NMR(δppm, DMSO-d_6) 1.13-1.78(11H, m), 1.93-2.40(4H, m), 2.88(1.73H, s), 2.99(1.27H, s), 3.22(1H, m), 4.05(0.43H, d, J=7.0Hz), 4.21(0.57H, d, J=7.0Hz), 4.51(0.57H, m), 4.76(0.43H, m), 7.49-7.68(4H, m), 7.83(2H, m), 8.08(3H, brs).
Example 86		^{1}H-NMR(δppm, DMSO-d_6) 1.25-1.85(11H, m), 1.93-2.39(4H, m), 2.91(1.78H, s), 3.03(1.22H, s), 3.79(1H, m), 4.12(0.41H, d, J=6.5Hz), 4.28(0.59H, d, J=6.5Hz), 4.59(0.59H, m), 4.80(0.59H, m), 6.71(1H, m), 6.86(1H, t, J=7.4Hz), 7.20(2H, t, J=7.9Hz), 7.37(2H, d, J=8.3Hz), 8.12(3H, brs).

Table 1—23

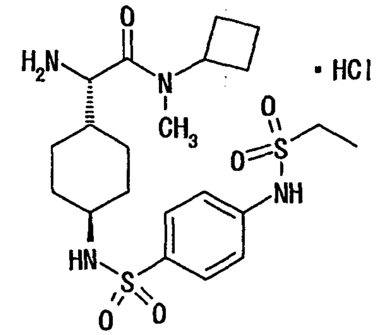
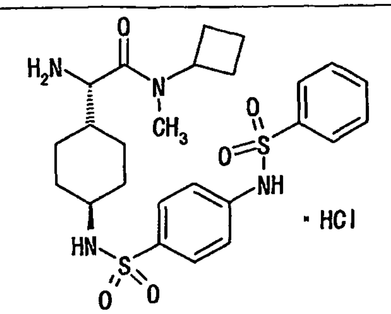
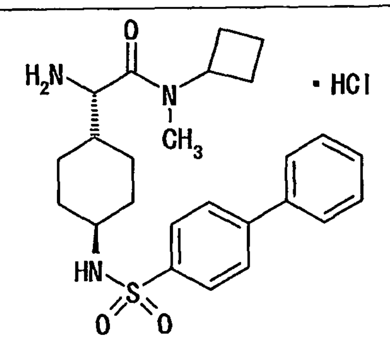
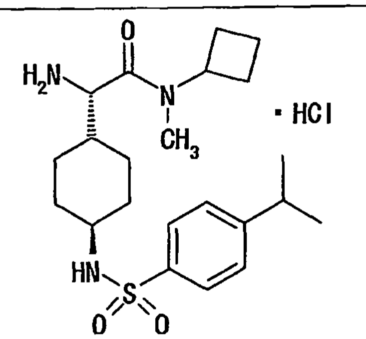
Example 87		^{1}H-NMR(δppm, DMSO-d_6) 0.94-1.30(7H, m), 1.17-1.75(7H, m), 1.92-2.37(4H, m), 2.78(1H, m), 2.86(1.65H, s), 2.93(1.35H, s), 3.22(2H, q, J=7.3Hz), 4.07(0.45H, m), 4.21(0.55H, m), 4.46(0.55H, m), 4.72(0.45H, m), 7.34(2H, d, J=8.8Hz), 7.59(1H, m), 7.73(2H, d, J=8.8Hz), 7.99(3H, brs), 10.37(1H, s).
Example 88		^{1}H-NMR(δppm, DMSO-d_6) 0.89-1.28(4H, m), 1.38-1.74(7H, m), 1.93-2.40(4H, m), 2.71(1H, m), 2.86(1.73H, s), 2.96(1.27H, s), 4.07(0.42H, m), 4.23(0.58H, m), 4.48(0.58, m), 4.75(0.42H, m), 7.25(2H, d, J=8.8Hz), 7.46-7.70(6H, m), 7.80(2H, d, J=8.8Hz), 8.01(3H, brs).
Example 89		^{1}H-NMR(δppm, DMSO-d_6) 0.92-1.32(4H, m), 1.40-1.79(7H, m), 1.88-2.34(4H, m), 2.77-3.02(4H, m), 4.06(0.45H, d, J=5.6Hz),4.20(0.55H, d, J=5.6Hz), 4.46(0.55H, m), 4.72(0.45H, m), 7.44(1H, m), 7.52(2H, m), 7.69-7.80(3H, m), 7.81-8.12(7H, m).
Example 90		^{1}H-NMR(δppm, DMSO-d_6) 0.95-1.19(4H, m), 1.22(6H, d, J=6.5Hz), 1.40-1.78(7H, m), 1.92-2.40(4H, m), 2.70-3.07(5H, m), 4.06(0.45H, d, J=5.6Hz), 4.20(0.55H, d, J=5.6Hz), 4.47(0.55H, m), 4.73(0.45H, m), 7.45(2H, d, J=8.3Hz), 7.61(1H, m), 7.71(2H, d, J=8.3Hz), 7.93(3H, brs).

Table 1-24

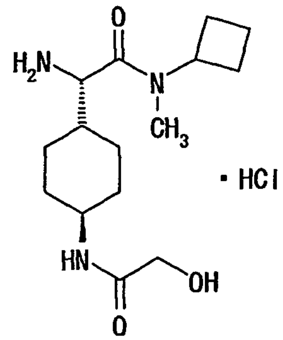
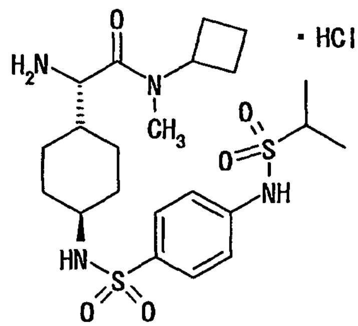
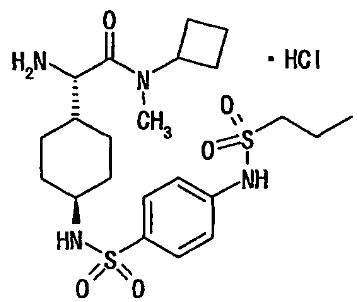
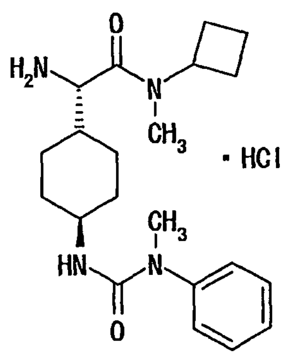
Example 91		^{1}H-NMR(δppm, DMSO-d_6) 1.06-1.36(4H, m), 1.44-1.85(7H, m), 1.93-2.39(4H, m), 2.88(1.78H, s), 2.99(1.22H, s), 3.51(1H, m), 3.75(2H, d, J=5.6Hz), 4.14(0.41H, d, J=5.6Hz), 4.29(0.59H, d, J=5.6Hz), 4.53(0.59H, m), 4.77(0.41H, m), 5.44(1H, m), 7.48(1H, m), 8.02(3H, brs).
Example 92		^{1}H-NMR(δppm, DMSO-d_6) 0.95-1.20(4H, m), 1.26(6H, d, J=7.0Hz), 1.41-1.77 (7H, m), 1.92-2.39(4H, m), 2.76(1H, s), 2.86(1.70H, s), 2.95(1.30H, s), 3.36(1H, sep, J=7.0Hz), 4.08(0.43H, m), 4.23(0.57H, m), 4.47(0.57H, m), 4.73(0.43H, m), 7.35(2H, d, J=8.8Hz), 7.58(1H, m), 7.72(2H, d, J=8.8Hz), 7.90(3H, brs), 10.32(1H, s).
Example 93		^{1}H-NMR(δppm, DMSO-d_6) 0.94(3H, t, J=7.4Hz), 0.98-1.21(4H, m), 1.39-1.80 (9H, m), 1.92-2.38(4H, m), 2.69- 3.00(4H, m), 3.19(2H, t, J=7.4Hz), 4.07(0.45H, m), 4.22(0.55H, m), 4.4(0.55H, m), 4.72(0.45H, m), 7.33(2H, d, J=8.8Hz), 7.59(1H, m), 7.73(2H, d, J=8.8Hz), 8.00(3H, brs), 10.38(1H, s).
Example 94		^{1}H-NMR(δppm, DMSO-d_6) 1.02-1.35(4H, m), 1.44-1.86(7H, m), 1.92-2.40(4H, m), 2.88(1.80H, s), 2.97(1.20H, s), 3.13(3H, s), 3.36(1H, m), 4.14(0.40H, m), 4.29(0.60H, m), 4.52(0.60H, m), 4.76(0.40H, m), 5.66(1H, m), 7.12-7.26(3H, m), 7.35(2H, m), 8.08(3H, brs).

Table 1—25

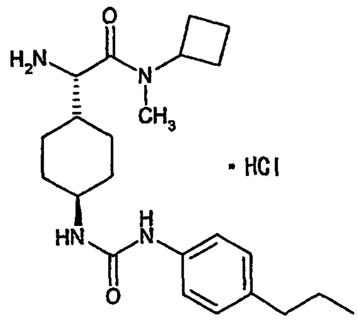
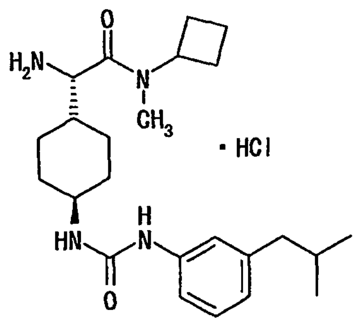
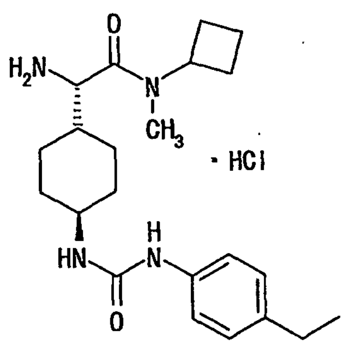
Example 95		^{1}H-NMR(δppm, DMSO-d_6) 0.87(3H, t, J=7.1Hz), 0.96-1.40(4H, m), 1.42-1.80 (7H, m), 1.81-2.36(6H, m), 2.45(2H, t, J=7.4Hz), 2.90(1.74H, s), 3.01(1.26H, s), 3.35(1H, m), 4.17(0.42H, d, J=5.6Hz), 4.31(0.58H, d, J=5.6Hz), 4.55(0.58H, m), 4.76(0.42H, m), 6.16(1H, d, J=7.4Hz), 7.00(2H, d, J=8.3Hz), 7.25(2H, d, J=8.3Hz), 8.07(3H, brs), 8.44(1H, s).
Example 96		^{1}H-NMR(δppm, DMSO-d_6) 0.85(6H, d, J=6.5Hz), 0.96-1.40(4H, m), 1.47-2.43 (14H, m), 2.89(1.73H, s), 2.99(1.27H, s), 3.33(1H, m), 4.17(0.42H, m), 4.32 (0.58H, m), 4.54(0.58H, m), 4.77 (0.42H, m), 6.22(1H, d, J=7.4Hz), 6.65(1H, d, J=7.4Hz), 7.08(1H, t, J=7.4Hz), 7.12-7.19(2H, m), 8.09(3H, brs), 8.51(1H, s).
Example 97		^{1}H-NMR(δppm, DMSO-d_6) 0.92-1.42(7H, m), 1.51-1.80(5H, m), 1.83-2.39(6H, m), 2.50(2H, q, J=7.1Hz), 2.89(1.72H, s), 2.99(1.28H,s), 3.52(1H, m), 4.17 (0.43H, m), 4.31(0.57H, m), 4.54 (0.57H, m), 4.77(0.43H, m), 6.22(1H, m), 7.02(2H, d, J=8.3Hz), 7.25(2H, d, J=8.3Hz), 8.12(3H, brs), 8.51(1H, s).

Table 1—26

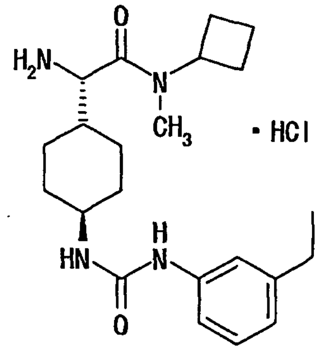
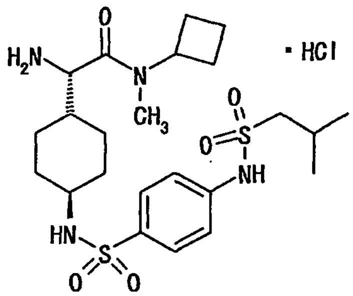
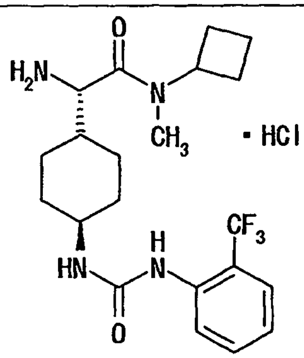
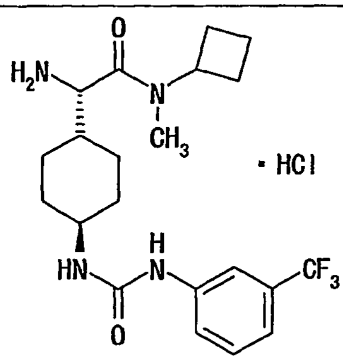
Example 98		^{1}H-NMR(δppm, DMSO-d_6) 0.95-1.42(7H, m), 1.48-1.79(5H, m), 1.83-2.39(6H, m), 2.53(2H, q, J=7.1Hz), 2.89(1.72H, s), 3.00(1.28H, s), 3.33(1H, m), 4.17(0.43H, m), 4.30(0.57H, m), 4.55(0.57H, m), 4.77(0.43H, m), 6.25(1H, d, J=7.9Hz), 6.71(1H, d, J=7.4Hz), 7.03-7.25(3H, m), 8.11(3H, brs), 8.55(1H, s).
Example 99		^{1}H-NMR(δppm, DMSO-d_6) 0.87-1.30(10H, m), 1.39-1.78(7H, m), 1.88-2.40(5H, m), 2.70-3.00(4H, m), 3.11(2H, d, J=6.5Hz), 4.07(0.44H, m), 4.21(0.56H, m), 4.47(0.56H, m), 4.72(0.44H, m), 7.32(2H, d, J=8.8Hz), 7.59(1H, m), 7.73(2H, d, J=8.8Hz), 8.04(3H, brs), 10.41(1H, s).
Example 100		^{1}H-NMR(δppm, DMSO-d_6) 0.87-1.43(4H, m), 1.50-1.77(5H, m), 1.87-2.40(6H, m), 2.89(1.72H, s), 3.00(1.28H, s), 3.32(1H, m), 4.16(0.43H, m), 4.30(0.57H, m), 4.54(0.57H, m), 4.76(0.43H, m), 7.06(1H, d, J=7.4Hz), 7.15(1H, t, 7.7Hz), 7.52-7.62(2H, m), 7.94(1H, d, J=8.3Hz), 8.12(3H, brs).
Example 101		^{1}H-NMR(δppm, DMSO-d_6) 0.97-1.43(4H, m), 1.45-1.79(5H, m), 1.83-2.40(6H, m), 2.90(1.73H, s), 3.00(1.27H, s), 3.33(1H, m), 4.17(0.42H, m), 4.31(0.58H, m), 4.54(0.58H, m), 4.70(0.42H, m), 6.44(1H, d, J=7.4Hz), 7.19(1H, d, J=7.4Hz), 7.35-7.50(2H, m), 7.95(1H, s), 8.09(3H, brs), 9.14(1H, s).

Table 1—27

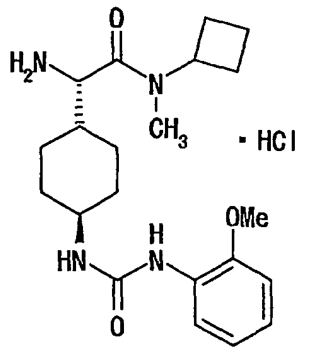
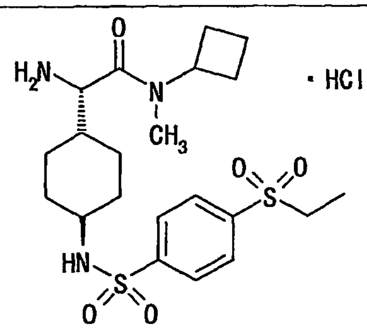
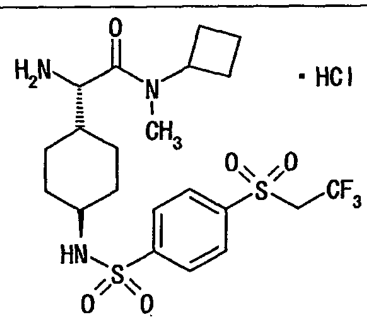
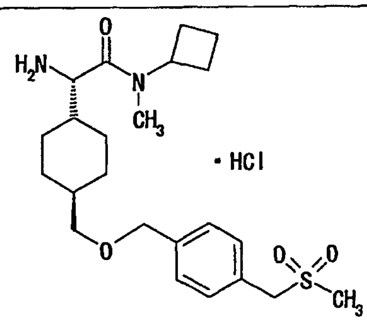
Example 102		^{1}H-NMR(δppm, DMSO-d_6) 0.88-1.41(4H, m), 1.49-1.79(5H, m), 1.82-2.40(6H, m), 2.90(1.68H, s), 3.00(1.32H, s), 3.81(3H, s), 4.17(0.44H, m), 4.31(0.56H, m), 4.54(0.56H, m), 4.77(0.44H, m), 6.74-6.88(3H, m), 6.93(1H, m), 7.79(1H, m), 7.97-8.21(4H, m).
Example 103		^{1}H-NMR(δppm, DMSO-d_6) 0.93-1.27(7H, m), 1.40-1.77(8H, m), 2.77-3.00(4H, m), 3.38(2H, q, J=7.4Hz), 4.05(0.45H, d, J=5.1Hz), 4.20(0.55H, d, J=5.1Hz), 4.45(0.55H, m), 4.71(0.45H, m), 7.88-8.14(8H, m).
Example 104		^{1}H-NMR(δppm, DMSO-d_6) 0.95-1.25(4H, m), 1.41-1.76(7H, m), 1.91-2.37(4H, m), 2.79-3.00(4H, m), 4.06(0.47H, d, J=5.1Hz), 4.21(0.53H, d, J=5.1Hz), 4.45(0.53H, m), 4.71(0.47H, m), 5.11(2H, q, J=9.9Hz), 7.80-8.32(8H, m).
Example 105		^{1}H-NMR(DMSO-d_6) 0.78-1.26(4H, m), 1.39-1.86(7H, m), 1.93-2.37(5H, m), 2.85-2.91(4.71H, m), 2.96(1.29H, s), 3.22(2H, d, J=6.0Hz), 4.13(0.43H, m), 4.28(0.57H, m), 4.40-4.57(4.57H, m), 4.75(0.43H, m), 7.26-7.11(4H, m), 8.05(3H, brs).

Table 1—28

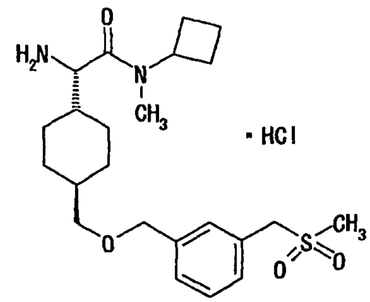
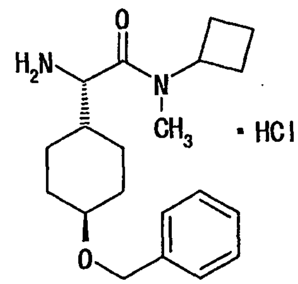
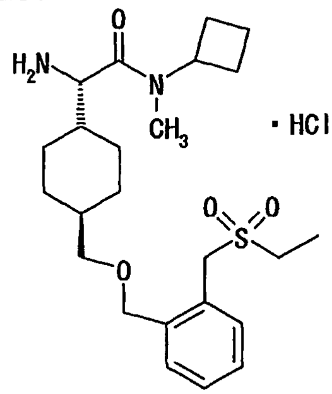
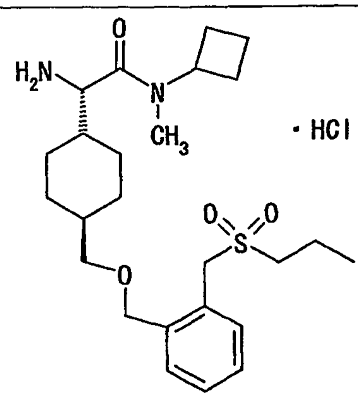
Example 106		^{1}H-NMR(δppm, DMSO-d_6) 0.76-1.26(3H, m), 1.40-1.87(8H, m), 1.92-2.36(5H, m), 2.84-2.91(4.76H, m), 2.97(1.24H, s), 3.22(2H, d, J=6.0Hz), 4.13(0.41H, d, J=5.1Hz), 4.28(0.59H, d, J=5.1z), 4.37-4.59(4.59H, m), 4.75(0.41H, m), 7.22-7.43(4H, m), 8.05(3H, brs).
Example 107		^{1}H-NMR(δppm, DMSO-d_6) 0.97-1.31(4H, m), 1.48-1.78(5H, m), 1.92-2.36(6H, m), 2.87(1.80H, s), 2.98(1.20H, s), 3.20(1H, m), 4.12(0.40H, d, J=5.6Hz), 4.28(0.60H, d, J=5.6Hz), 4.41-4.58(2.60H, m), 4.75(0.40H, m), 7.09-7.41(5H, m), 8.13(3H, brs).
Example 108		^{1}H-NMR(δppm, DMSO-d_6) 0.73-1.32(7H, m), 1.38-1.87(8H, m), 1.92-2.40(4H, m), 2.88(1.71H, s), 2.97(1.29H, s), 3.12(2H, q, J=7.4Hz), 3.24(2H, d, J=6.0Hz), 4.14(0.43H, d, J=5.1Hz), 4.29(0.57H, d, J=5.1Hz), 4.43-4.66(4.57H, m), 4.76(0.3H, m), 7.25-7.47(4H, m), 8.05(3H, brs).
Example 109		^{1}H-NMR(δppm, DMSO-d_6) 0.76-1.30(7H, m), 1.37-1.86(10H, m), 1.92-2.38(4H, m), 2.88(1.70H, s), 2.97(1.30H, s), 3.04-3.14(2H, m), 3.23(2H, d, J=6.0Hz), 4.14(0.43H, m), J=5.1Hz), 4.29(0.57H, d, J=5.1Hz), 4.47-4.63(4.57H, m), 4.76(0.43H, m), 7.28-7.49(4H, m), 8.03(4H, brs).

Table 1—29

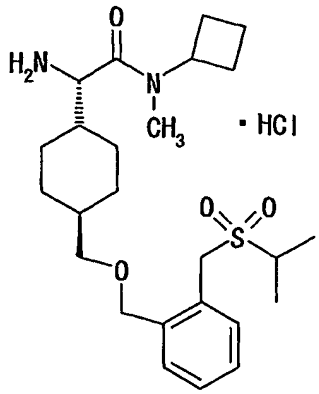
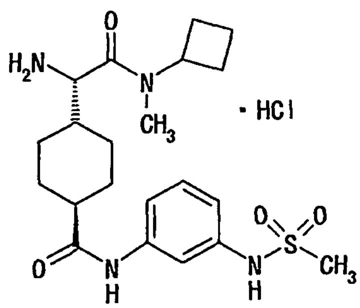
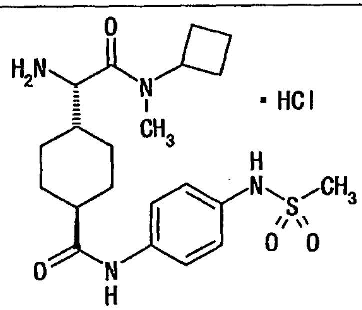
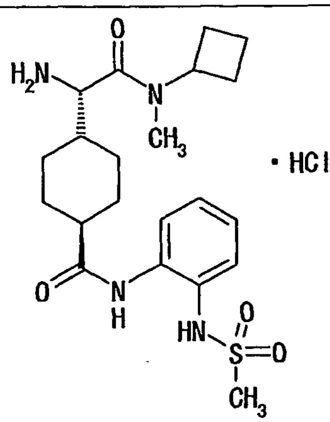
Example 110		^{1}H-NMR(δppm, DMSO-d_6) 0.78-1.35(10H, m), 1.38-1.87(8H, m), 1.92-2.38(4H, m), 2.88(1.73H, m), 2.97(1.27H, s), 3.23(2H, d, J=6.5Hz), 3.34(1H, sep, J=7.4Hz), 4.14(0.42H, d, J=5.6Hz), 4.29(0.58H, d, J=5.6Hz), 4.45-4.64(4.58H, m), 4.77(0.42H, m), 7.27-7.44(4H, m), 8.06(3H, brs).
Example 111		^{1}H-NMR(δppm, DMSO-d_6) 1.04-1.49(4H, m), 1.54-1.93(7H, m), 1.94-2.40(5H, m), 2.90(1.72H, s), 2.96(3H, s), 3.00(1.28H, s), 4.21(0.43H, m), 4.35(0.57H, m), 4.56(0.57H, m), 4.78(0.43H, m), 6.84(1H, d, J=7.9Hz), 7.20(1H, t, J=8.1Hz), 7.36(1H, d, J=8.8Hz), 7.53(1H, s), 8.05(3H, brs), 9.72(1H, brs), 9.92(1H, s).
Example 112		^{1}H-NMR(δppm, DMSO-d_6) 1.06-1.51(4H, m), 1.55-1.94(7H, m), 1.96-2.40(5H, m), 2.89(4.81H, s), 3.00(1.19H, s), 4.19(0.40H, m), 4.33(0.60H, m), 4.55(0.60H, m), 4.78(0.40H, m), 7.12(2H, d, J=8.8Hz), 7.54(2H, d, J=8.8Hz), 7.96(3H, brs), 9.53(1H, brs), 9.85(1H, s).
Example 113		^{1}H-NMR(δppm, DMSO-d_6) 1.11-1.50(4H, m), 1.52-1.84(5H, m), 1.87-2.42(7H, m), 2.90(1.80H, s), 2.92(3H, s), 3.00 (1.20H, s), 4.20(0.40H, d, J=5.6Hz), 4.35(0.60H, d, J=5.6Hz), 4.56(0.60H, m), 4.78(0.40H, m), 7.12-7.27(2H, m), 7.35(1H, d, J=6.5Hz), 7.64(1H, d, J=6.5Hz), 8.08(3H, brs), 9.54(1H, s).

Table 1—30

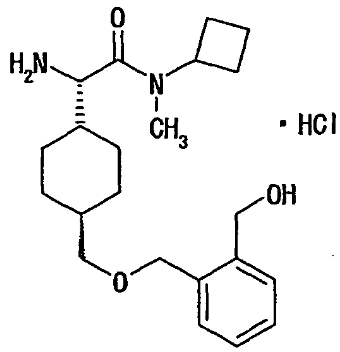
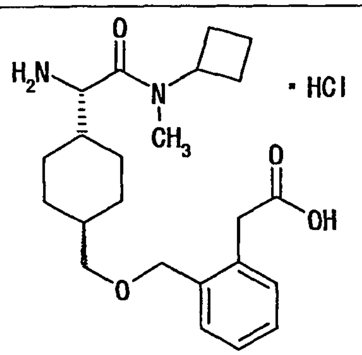
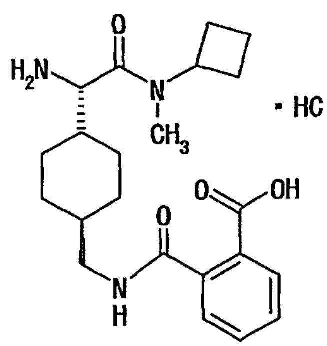
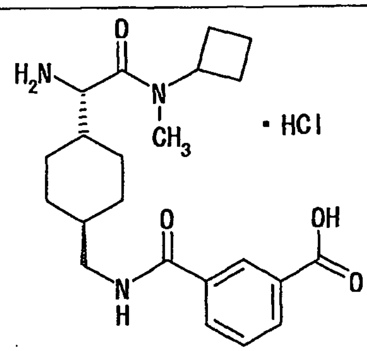
Example 114		^{1}H-NMR(δppm, DMSO-d_6) 0.74-1.31(4H, m), 1.32-1.85(8H, m), 1.91-2.37(4H, m), 2.88(1.72H, s), 2.97(1.28H, s), 3.22(2H, d, J=6.0Hz), 4.14(0.43H, m), 4.29(0.57H, m), 4.41-4.59(4.57H, m), 4.76(0.43H, m), 5.06(1H, brs), 7.16-7.48(4H, m), 8.05(3H, brs).
Example 115		^{1}H-NMR(δppm, DMSO-d_6) 0.71-1.29(4H, m), 1.32-1.86(8H, m), 1.88-2.38(4H, m), 2.87(1.76H, s), 2.96(1.24H, s), 3.19(2H, d, J=5.6Hz), 3.61(2H, s), 4.12(0.41H, m), 4.26(0.59H, m), 4.33-4.60(2.59H, m), 4.75(0.41H, m), 7.00-7.45(4H, m), 8.10(3H, brs).
Example 116		^{1}H-NMR(δppm, DMSO-d_6) 0.75-1.28(4H, m), 1.33-1.89(8H, m), 1.92-2.39(4H, m), 2.89(1.73H, s), 2.93-3.09 (3.27H, m), 4.15(0.42H, d, J=5.6Hz), 4.30(0.58H, d, J=5.6Hz), 4.53(0.58H, m), 4.77(0.42H, m), 7.38(1H, d, J=7.4Hz), 7.44-7.58(2H, m), 7.73(1H, d, J=7.4Hz), 8.04(3H, brs), 8.28(1H, t, J=5.6Hz).
Example 117		^{1}H-NMR(δppm, DMSO-d_6) 0.75-1.30(4H, m), 1.36-1.87(8H, m), 1.91-2.39(4H, m), 2.88(1.73H, m), 2.97(1.27H, s), 3.09(2H, m), 4.15(0.42H, m), 4.30(0.58H, m), 4.52(0.58H, m), 4.76(0.42H, m), 7.58(1H, t, J=7.9Hz), 7.87-8.21(4H, m), 8.40(1H, m), 8.67(1H, m).

Table 1-31

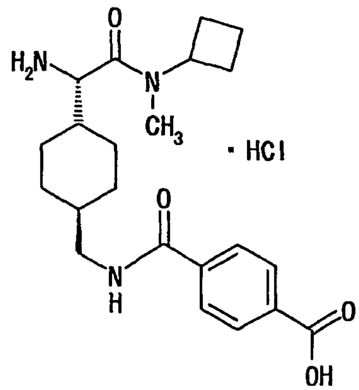
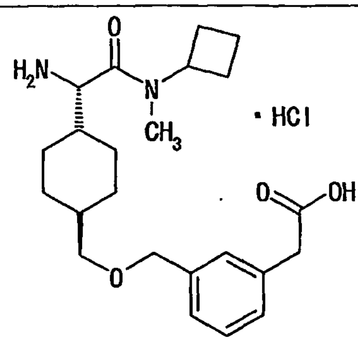
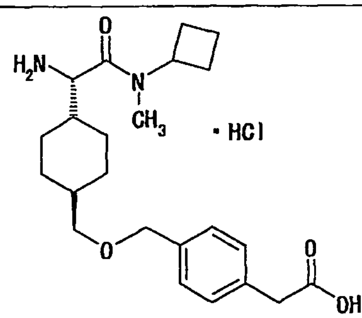
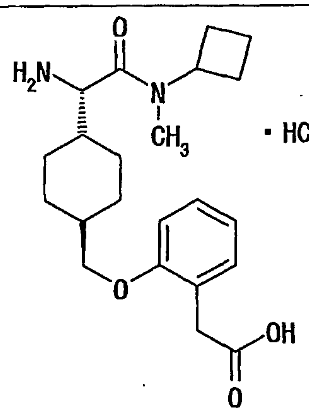
Example 118		^{1}H-NMR(δppm, DMSO-d_6) 0.76-1.27(4H, m), 1.38-1.86(8H, m), 1.91-2.38(4H, m), 2.89(1.77H, s), 2.97(1.23H, s), 3.01(2H, m), 4.14(0.41H, m), 4.29(0.59H, m), 4.52(0.59H, m), 4.75(0.41H, m), 7.92(2H, d, J=7.9Hz), 7.99(2H, d, J=7.9Hz), 8.05(3H, brs), 8.64(1H, t, J=5.8Hz), 13.18(1H, brs).
Example 119		^{1}H-NMR(δppm, DMSO-d_6) 0.70-1.33(4H, m), 1.36-1.91(8H, m), 1.92-2.40(4H, m), 2.88(1.70H, s), 2.97(1.30H, s), 3.22(2H, brs), 3.55(2H, s), 4.13(0.43H, m), 4.28(0.57H, m), 4.34-4.63(2.57H, m), 4.76(0.43H, m), 7.04-7.45(7H, m).
Example 120		^{1}H-NMR(δppm, DMSO-d_6) 0.73-1.28(4H, m), 1.31-1.86(8H, m), 1.88-2.37(4H, m), 2.88(1.75H, s), 2.97(1.25H, s), 3.20(2H, d, J=6.5Hz), 3.54(2H, s), 4.13(0.42H, d, J=5.1Hz), 4.28(0.58H, d, J=5.1Hz), 4.40(2H, s), 4.52(0.58H, m), 4.76(0.42H, m), 7.22(4H, m).
Example 121		^{1}H-NMR(δppm, DMSO-d_6) 0.94-1.31(4H, m), 1.49-1.76(6H, m), 1.77-1.91(2H, m), 1.77-2.37(4H, m), 2.89(1.79H, s), 2.99(1.21H, s), 3.47(2H, s), 3.75(2H, d, J=5.6Hz), 4.15(0.40H, d, J=5.6Hz), 4.31(0.60H, d, J=5.6Hz), 4.53(0.60H, m), 4.78(0.40H, m), 6.79-6.94(2H, m), 7.10-7.26(2H, m), 8.08(3H, brs).

Table 1-32

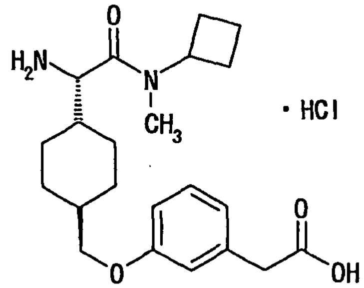
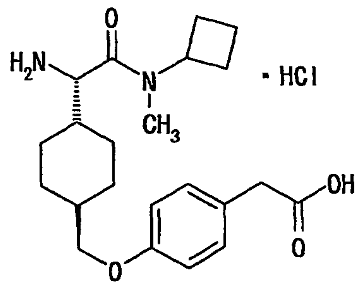
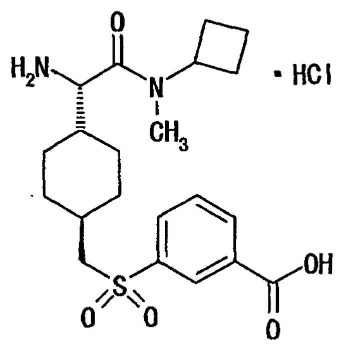
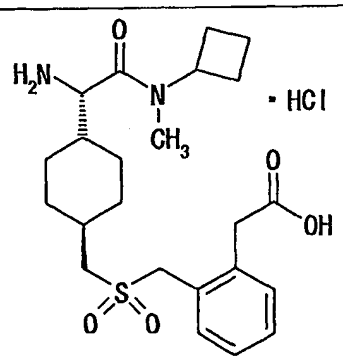
Example 122		^{1}H-NMR(δppm, DMSO-d_6) 0.84-1.37(4H, m), 1.48-1.78(6H, m), 1.79-2.40(6H, m), 2.89(1.76H, s), 2.98(1.24H, s), 3.51(2H, s), 3.74(2H, d, J=6.0Hz), 4.16(0.41H, m), 4.29(0.59H, m), 4.54(0.59H, m), 4.78(0.41H, m), 6.71-6.87(3H, m), 7.19(1H, t, J=7.9Hz).
Example 123		^{1}H-NMR(δppm, DMSO-d_6) 0.83-1.33(4H, m), 1.49-1.77(6H, m), 1.78-2.39(6H, m), 2.88(1.74H, s), 2.98(1..26H, s), 3.46(2H, s), 3.74(2H, d, J=6.0Hz), 4.15(0.42H, d, J=5.1Hz), 4.29(0.58H, d, J=5.1Hz), 4.54(0.58H, m), 4.77(0.42H, m), 6.83(2H, d, J=7.9Hz), 7.13(2H, d, J=7.9Hz), 8.17(3H, brs).
Example 124		^{1}H-NMR(δppm, DMSO-d_6) 0.91-1.30(4H, m), 1.44-1.75(6H, m), 1.77-2.37(6H, m), 2.87(1.76H, s), 2.95(1.24H, s), 3.29(2, d, J=6.5Hz), 4.11(0.41H, d, J=5.1Hz), 4.25(0.59H, d, J=5.1Hz), 4.50(0.59H, m), 4.75(0.41H, m), 7.80(1H, t, J=7.9Hz), 8.06(3H, brs), 8.13(1H, d, J=7.9Hz), 8.26(1H, d, J=7.9Hz), 8.36(1H, s).
Example 125		^{1}H-NMR(δppm, DMSO-d_6) 0.91-1.33(4H, m), 1.49-1.72(5H, m), 1.75-2.37(7H, m), 2.88(1.74H, s), 2.97(1.26H, s), 3.08(2H, d, J=6.5Hz), 3.76(2H, s,), 4.13(0.41H, d, J=5.1Hz) 4.28(0.59H, d, J=5.1Hz), 4.44-4.60(2.59H, m), 4.76(0.41H, m), 7.22-7.40(4H, m).

Table 1-33

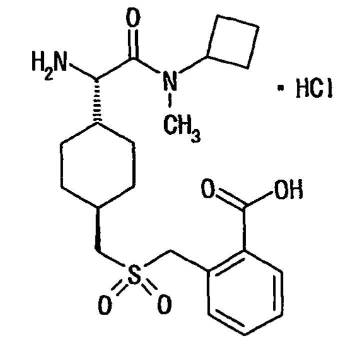
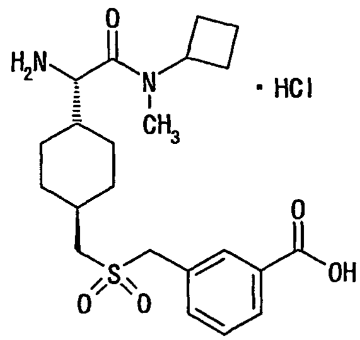
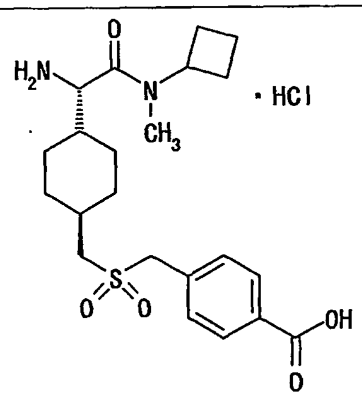
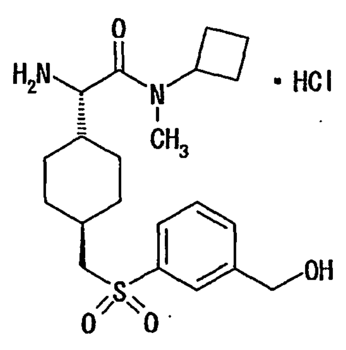
Example 126		^{1}H-NMR(δppm, DMSO-d_6) 0.88-1.33(4H, m), 1.46-2.38(12H, m), 2.88(1.74H, s), 2.94(2H, d, J=6.0Hz), 2.96(1.26H, s), 4.12(0.41H, d, J=5.1Hz), 4.27(0.59H, d, J=5.1Hz), 4.51(0.59H, m), 4.76(0.41H, m), 5.00(2H, s), 7.43-7.54(2H, m), 7.58(1H, m), 7.90(1H, m).
Example 127		^{1}H-NMR(δppm, DMSO-d_6) 0.91-1.30(4H, m), 1.49-1.71(5H, m), 1.73-2.37(7H, m), 2.88(1.76H, m), 2.93-3.00(3.24H, m), 4.12(0.42H, d, J=5.6Hz), 4.27 (0.58H, d, J=5.6Hz), 4.44-4.64 (2.58H, m), 4.75(0.42H, m), 7.53(1H, t, J=7.7Hz), 7.62(1H, d, J=7.9Hz), 7.94(1H, t, J=7.4Hz), 7.99(1H, s).
Example 128		^{1}H-NMR(δppm, DMSO-d_6) 0.89-1.31(4H, m), 1.49-1.71(5H, m), 1.73-2.37(7H, m), 2.87(1.74H, s), 2.90-3.02(3.26H, m), 4.12(0.42H, d, J=5.1Hz), 4.27(0.58H, d, J=5.1Hz), 4.44-4.64 (2.58H, m), 4.76(0.42H, m), 7.51(2H, d, J=8.3Hz), 7.95(2H, d, J=8.3Hz).
Example 129		^{1}H-NMR(δppm, DMSO-d_6) 0.89-1.28(4H, m), 1.45-1.75(6H, m), 1.77-2.37(6H, m), 2.87(1.76H, s), 2.95(1.24H, s), 3.19(2H, d, J=6.0Hz), 4.10(0.41, d, J=5.6Hz), 4.25(0.59H, d, J=5.6Hz), 4.50 (0.59H, m), 4.60(2H, d, J=6.0Hz), 4.75(0.41H, m), 5.47(1H, t, J=6.0Hz), 7.60(1H, t, J=7.7Hz), 7.66(1H, d, J=7.9Hz), 7.75(1H, d, J=7.4Hz), 7.84(1H, s), 7.96(3H, brs).

Table 1-34

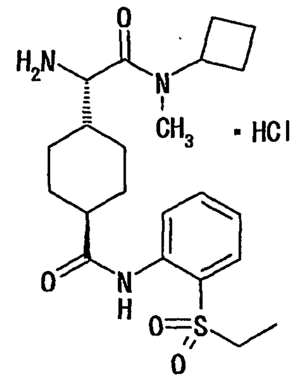
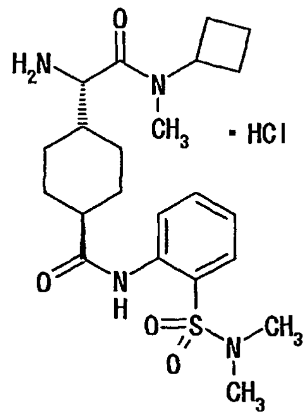
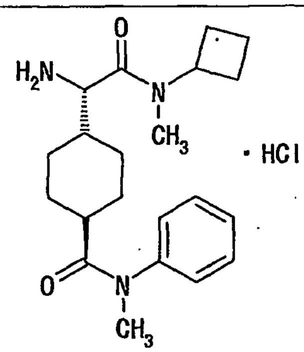
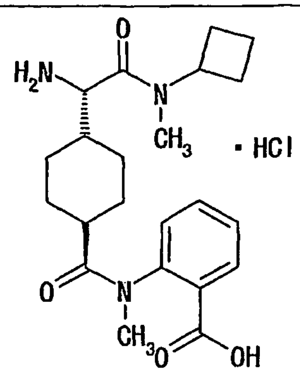
Example 130		^{1}H-NMR(δppm, DMSO-d_6) 1.08(3H, t, J=7.2Hz), 1.12-1.48(4H, m), 1.51-1.83(5H, m), 1.88-2.39(7H, m), 2.90(1.76H, s), 3.00(1.24H, s), 3.37(2H, q, J=7.2Hz), 4.18(0.41H, d, J=5.1Hz), 4.33(0.59H, d, J=5.1Hz), 4.55(0.59H, m), 4.78(0.41H, m), 7.40(1H, m), 7.72(1H, m), 7.84(1H, m), 8.00-8.16(4H, brs), 9.64(1H, s).
Example 131		^{1}H-NMR(δppm, DMSO-d_6) 1.11-1.48(4H, m), 1.52-1.83(5H, m), 1.88-2.37(7H, m), 2.63(6H, s), 2.90(1.72H, s), 3.00(1.28H, s), 4.17(0.43H, d, J=5.6Hz), 4.33(0.57H, d, J=5.6Hz), 4.55(0.57H, m), 4.78(0.43H, m), 7.35(1H, m), 7.67(1H, m), 7.74(1H, d, J=7.9Hz), 8.04(3H, brs), 8.16(1H, d, J=7.9Hz), 9.55(1H, s).
Example 132		^{1}H-NMR(δppm, DMSO-d_6) 0.63-1.00(2H, m), 1.16-1.80(8H, s), 1.86-2.35(6H, m), 2.82(1.72H, s), 2.89(1.28H, s), 3.08(3H, s), 4.02(0.43H, m), 4.15(0.57H, m), 4.44(0.57H, m), 4.70(0.43H, m), 7.15-7.64(5H, m), 7.96(3H, brs).
Example 133		^{1}H-NMR(δppm, DMSO-d_6) 0.61-1.03(2H, m), 1.12-1.74(8H, m), 1.76-2.37(6H, m), 2.83(1.69H, s), 2.89(1.31H, s), 3.02(3H, s), 4.01(0.44H, m), 4.15(0.56H, m), 4.42(0.56H, m), 4.71(0.44H, m), 7.42(1H, d, J=7.7Hz), 7.51(1H, t, J=7.7Hz), 7.66(1H, t, J=7.7Hz), 7.83-7.99(4H, m).

Table 1-35

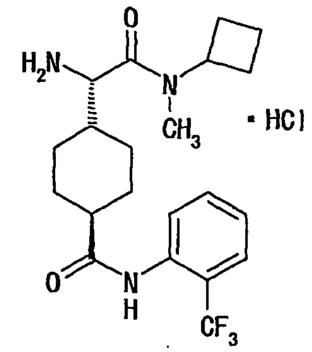
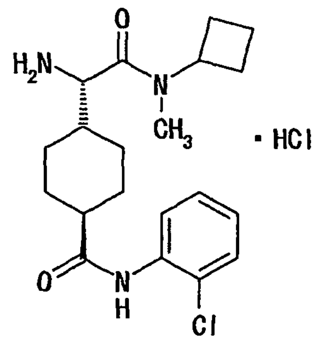
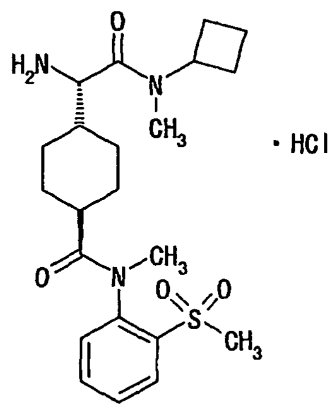
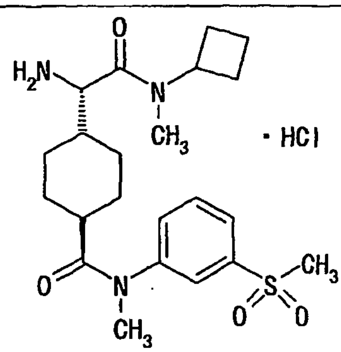
Example 134		[1]H-NMR(δppm, DMSO-d_6) 1.03-1.46(4H, m), 1.51-1.80(5H, m), 1.81-2.40(7H, m), 2.89(1.72H,s), 2.99(1.28H, s), 4.19(0.43H, d, J=5.1Hz), 4.34(0.57H, d, J=5.1Hz), 4.55(0.57H, m), 4.76(0.43H, m), 7.34-7.48(2H, m), 7.65(1H, t, J=7.7Hz), 7.71(1H, d, J=7.7Hz), 8.09(3H, brs), 9.49(1H, s).
Example 135		[1]H-NMR(δppm, DMSO-d_6) 1.03-1.49(4H, m), 1.53-1.81(5H, m), 1.82-2.43(7H, m), 2.89(1.72H, s), 2.99(1.28H, s), 4.19(0.43H, d, J=5.1Hz), 4.34(0.57H, d, J=5.1Hz), 4.55(0.57H, m), 4.76(0.43H, m), 7.17(1H, t, J=7.9Hz), 7.29(1H, t, J=7.9Hz), 7.46(1H, d, J=7.9Hz), 7.60(1H, d, J=7.9Hz), 8.09(3H, brs), 9.43(1H, s).
Example 136		[1]H-NMR(δppm, DMSO-d_6) 0.50-2.38(16H, m), 2.82(1.23H, s), 2.89(1.46H, s), 2.99(0.37H, s), 3.04(0.68H, s), 3.11(2.26H, s), 3.25(3H, s), 3.99(0.35H, d, J=5.1Hz), 4.07-4.19(0.65H, m), 4.25-4.86(1H, m), 7.38(0.27H, d, J=7.9Hz), 7.56-8.15(6.73H, m).
Example 137		[1]H-NMR(δppm, DMSO-d_6) 0.65-1.03(2H, m), 1.16-1.83(8H, m), 1.85-2.34(6H, m), 2.83(1.75H, s), 2.90(1.25H, s), 3.17(3H, brs), 3.25(3H, s), 4.03(0.42H, m), 4.17(0.58H, m), 4.44(0.58H, m), 4.70(0.42H, m), 7.64-7.78(2H, m), 7.80-8.06(5H, m).

Table 1-36

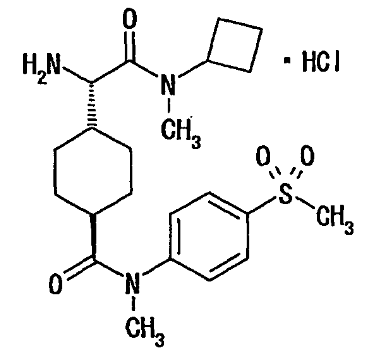
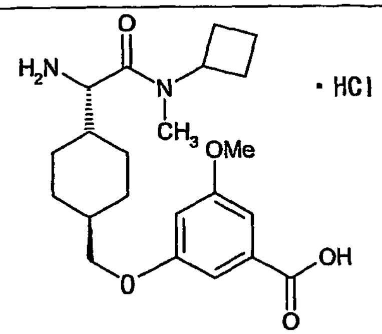
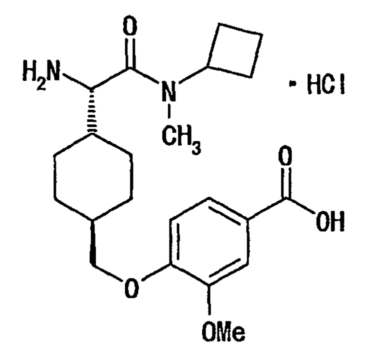
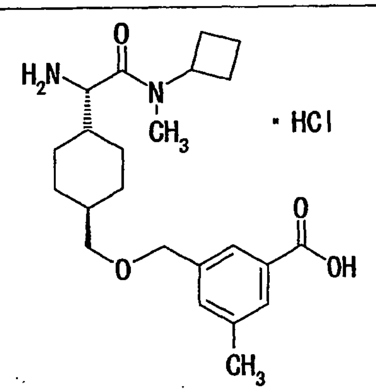
Example 138		^{1}H-NMR(δppm, DMSO-d_6) 0.77-1.12(2H, m), 1.17-1.83(8H, m), 1.86-2.35(6H, m), 2.83 (1.70H, s), 2.91(1.30H, s), 3.16(3H, brs), 3.25(3H, s), 4.03(0.43H, d, J=4.2Hz), 4.17(0.57H, m), 4.44(0.57H,m), 4.71(0.43H, m), 7.61(2H, d, J=8.3Hz), 7.93(3H, brs), 7.98(2H, d, J=8.3Hz).
Example 139		^{1}H-NMR(δppm, DMSO-d_6) 0.87-1.38(4H, m), 1.46-1.77(6H, m), 1.79-2.38(6H, m), 2.89(1.73H, s), 2.98(1.27H, s), 3.77(3H, s), 3.80(2H, d, J=6.5Hz), 4.15(0.42H, d, J=5.1Hz), 4.30(0.58H, d, J=5.1Hz), 4.54(0.58H, m), 4.77(0.42H, m), 6.70(1H, s), 6.99-7.06(2H, m), 8.09(3H, brs).
Example 140		^{1}H-NMR(δppm, DMSO-d_6) 0.88-1.38(4H, m), 1.48-1.77(6H, m), 1.79-2.38(6H, m), 2.89(1.69H, s), 2.98(1.31H, s), 3.79(3H, s), 3.82(2H, d, J=6.5Hz), 4.15(0.44H, d, J=5.1Hz), 4.30(0.56H, m), 4.54(0.56H, m), 4.77(0.44H, m), 7.01(1H, d, J=8.3Hz), 7.43(1H, d, J=1.9Hz), 7.52(1H, dd, J=8.3, 1.9Hz), 8.09(3H, brs).
Example 141		^{1}H-NMR(δppm, DMSO-d_6) 0.74-1.25(4H, m), 1.34-1.83(8H, m), 1.87-2.39(7H, m), 2.80(1.71H, s), 2.95(1.29H, s), 3.21(2H, d, J=6.0Hz), 4.11(0.43H, d, J=5.6Hz), 4.26(0.57H, d, J=5.6Hz), 4.43(2H, s), 4.50(0.57H, m), 4.73(0.43H, m), 7.32(1H, s), 7.65(2H, s), 8.06(3H, brs).

Table 1-37

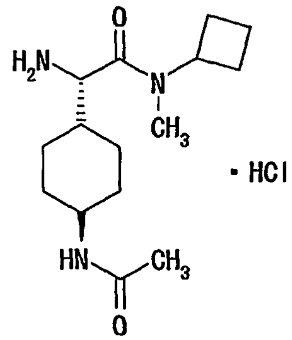
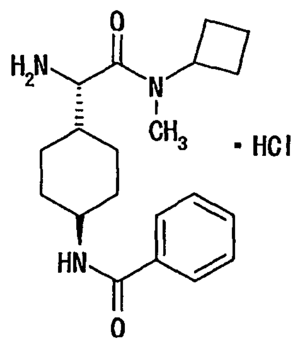
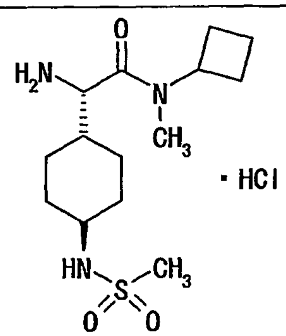
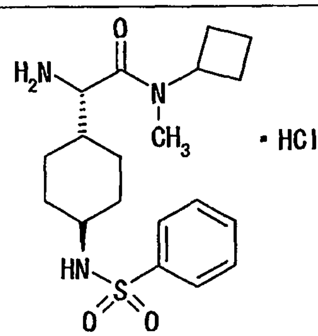
Example 142		^{1}H-NMR(δppm, DMSO-d_6) 0.92-1.32 (4H, m), 1.52-1.85 (7H, m), 1.94-2.36 (4H, m), 2.88 (1.74H, s), 2.98 (1.26H, s), 3.32-3.46 (1H, m), 4.09-4.17 (0.42H, m), 4.24-4.33 (0.58H, m), 4.47-4.59 (0.58H, m), 4.69-4.81 (0.42H, m), 7.73 (1H, brs), 8.13 (3H, brs).
Example 143		^{1}H-NMR(δppm, DMSO-d_6) 1.20-1.39 (4H, m), 1.58-1.76 (5H, m), 1.83-1.93 (2H, m), 1.97-2.36 (4H, m), 2.90 (1.74H, s), 3.00 (1.26H, s), 3.64-3.75 (1H, m), 4.14-4.19 (0.42H, m), 4.29-4.35 (0.58H, m), 4.51-4.61 (0.58H, m), 4.71-4.82 (0.42H, m), 7.43 (2H, dd, J=7.2, 7.2Hz), 7.49 (1H, d, J=7.2Hz), 7.81 (2H, d, J=7.2Hz), 8.13 (3H, brs), 8.22 (1H, m).
Example 144		^{1}H-NMR(δppm, DMSO-d_6) 1.06-1.32 (4H, m), 1.50-1.72 (5H, m), 1.86-2.36 (6H, m), 2.88 (1.74H, s), 2.89 (3H, s), 2.93-3.04 (1H, m), 2.97 (1.26H, s), 4.10-4.16 (0.42H, m), 4.25-4.31 (0.58H, m), 4.47-4.58 (0.58H, m), 4.69-4.80 (0.42H, m), 6.96-7.04 (1H, m), 8.11 (3H, brs).
Example 145		^{1}H-NMR(δppm, DMSO-d_6) 0.95-1.20 (4H, m), 1.43-1.70 (7H, m), 1.92-2.31 (4H, m), 2.74-2.87 (1H, m), 2.85 (1.74H, s), 2.92 (1.26H, s), 4.05 (0.42H, d, J=5.3Hz), 4.20 (0.58H, d, J=5.3Hz), 4.40-4.51 (0.58H, m), 4.65-4.76 (0.42H, m), 7.54-7.82 (5H, m), 8.03 (3H, brs).

Table 1-38

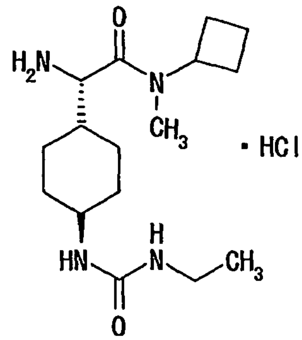
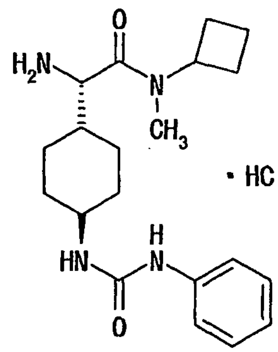
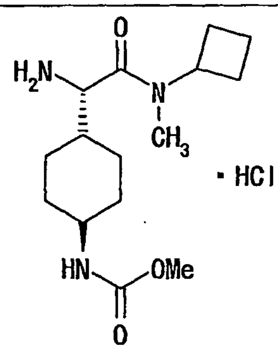
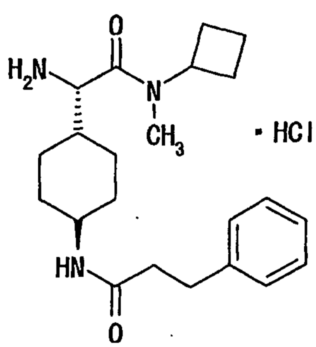
Example 146		^{1}H-NMR(δppm, DMSO-d$_6$) 0.90-1.32 (4H, m), 0.95 (3H, t, J=7.2Hz), 1.57-1.72 (5H, m), 1.76-1.87 (2H, m), 1.94-2.35 (4H, m), 2.88 (1.74H, s), 2.97 (2H, q, J=7.2Hz), 2.98 (1.26H, s), 3.17-3.27 (1H, m), 4.07-4.18 (0.42H, m), 4.23-4.34 (0.58H, m), 4.47-4.58 (0.58H, m), 4.69-4.80 (0.42H, m), 5.30-6.01 (2H, m), 8.09 (3H, brs).
Example 147		^{1}H-NMR(δppm, DMSO-d$_6$) 0.98-1.38 (4H, m), 1.53-1.77 (5H, m), 1.85-2.37 (6H, m), 2.89 (1.74H, s), 2.99 (1.26H, s), 3.26-3.45 (1H, m), 4.13-4.21 (0.42H, m), 4.26-4.35 (0.58H, m), 4.48-4.59 (0.58H, m), 4.70-4.82 (0.42H, m), 6.21 (2H, d, J=8.1Hz), 6.85 (1H, dd, J=7.2Hz, 7.2Hz), 7.18 (2H, dd, J=7.4, 7.2Hz), 7.35 (2H, d, J=7.4Hz), 8.08 (3H, brs), 8.55 (1H, s).
Example 148		^{1}H-NMR(δppm, DMSO-d$_6$) 1.01-1.32 (4H, m), 1.51-1.71 (5H, m), 1.75-1.86 (2H, m), 1.93-2.36 (4H, m), 2.88 (1.74H, s), 2.97 (1.26H, s), 3.08-3.20 (1H, m), 3.49 (3H, s), 4.13 (0.42H, d, J=5.1Hz), 4.28 (0.58H, d, J=5.1Hz), 4.47-4.58 (0.58H, m), 4.69-4.80 (0.42H, m), 6.98-7.08 (1H, m), 8.12 (3H, brs).
Example 149		^{1}H-NMR(δppm, DMSO-d$_6$) 0.92-1.30 (4H, m), 1.48-1.79 (7H, m), 1.92-2.34 (4H, m), 2.29 (2H, t, J=7.7Hz), 2.76 (2H, t, J=7.7Hz), 2.86 (1.74H, s), 2.96 (1.26H, s), 3.33-3.45 (1H, m), 4.06-4.15 (0.42H, m), 4.22-4.31 (0.58H, m), 4.45-4.56 (0.58H, m), 4.67-4.78 (0.42H, m), 7.09-7.27 (5H, m), 7.68 (1H, d, J=7.7Hz), 8.08 (3H, brs).

Table 1-39

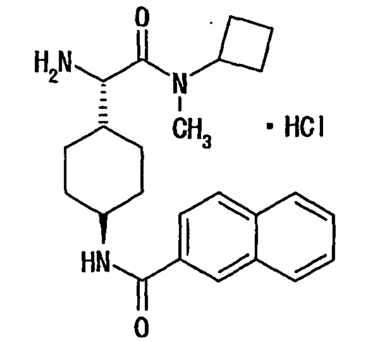
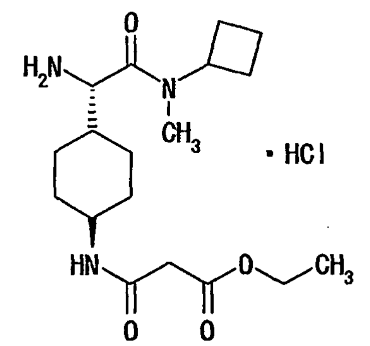
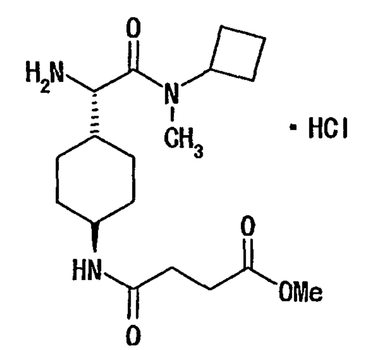
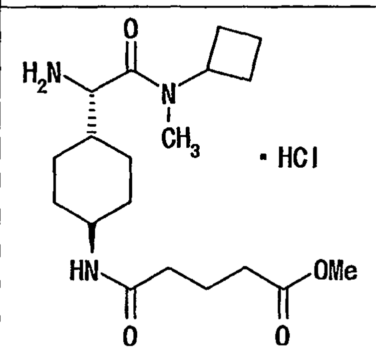
Example 150		^{1}H-NMR(δppm, DMSO-d_6) 1.19-1.43 (4H, m), 1.55-1.78 (5H, m), 1.84-2.36 (6H, m), 2.89 (1.74H, s), 3.00 (1.26H, s), 3.67-3.81 (1H, m), 4.13-4.21 (0.42H, m), 4.28-4.37 (0.58H, m), 4.50-4.62 (0.58H, m), 4.70-4.82 (0.42H, m), 7.51-7.62 (2H, m), 7.85-8.02 (4H, m), 8.11 (3H, brs), 8.33-8.44 (2H, m).
Example 151		^{1}H-NMR(δppm, DMSO-d_6) 0.97-1.34 (4H, m), 1.15 (3H, t, J=7.1Hz), 1.52-1.71 (5H, m), 1.74-1.85 (2H, m), 1.93-2.33 (4H, m), 2.87 (1.74H, s), 2.96 (1.26H, s), 3.13 (2H, s), 3.27-3.44 (1H, m), 4.03 (2H, q, J=7.1Hz), 4.09-4.17 (0.42H, m), 4.23-4.31 (0.58H, m), 4.45-4.56 (0.58H, m), 4.67-4.79 (0.42H, m), 7.94-8.01 (1H, m), 8.07 (3H, brs).
Example 152		^{1}H-NMR(δppm, DMSO-d_6) 0.96-1.30 (4H, m), 1.50-1.70 (5H, m), 1.71-1.82 (2H, m), 1.92-2.32 (4H, m), 2.28 (2H, t, J=6.9Hz), 2.45 (2H, t, J=6.9Hz), 2.86 (1.74H, s), 2.96 (1.26H, s), 3.31-3.43 (1H, m), 3.54 (3H, s), 4.08-4.16 (0.42H, m), 4.22-4.32 (0.58H, m), 4.45-4.57 (0.58H, m), 4.67-4.79 (0.42H, m), 7.70-7.78 (1H, m), 8.07 (3H, brs).
Example 153		^{1}H-NMR(δppm, DMSO-d_6) 0.95-1.30 (4H, m), 1.49-1.82 (9H, m), 1.92-2.34 (4H, m), 2.02 (2H, t, J=7.3Hz), 2.25 (2H, t, J=7.4Hz), 2.86 (1.74H, s), 2.96 (1.26H, s), 3.33-3.45 (1H, m), 3.55 (3H, s), 4.08-4.16 (0.42H, m), 4.22-4.31 (0.58H, m), 4.45-4.56 (0.58H, m), 4.67-4.79 (0.42H, m), 7.64-7.72 (1H, m), 8.07 (3H, brs).

Table 1-40

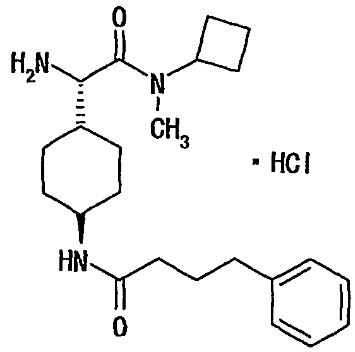
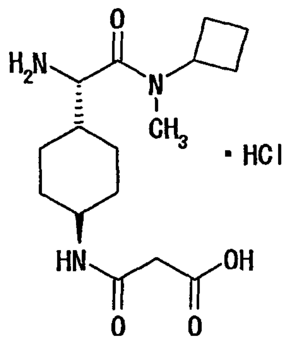
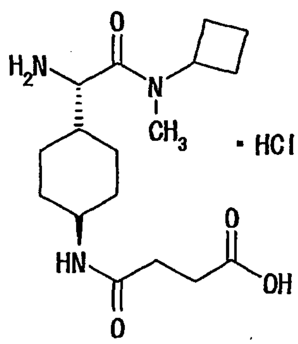
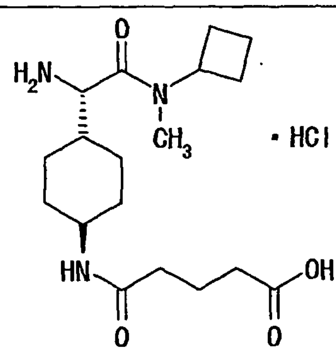
Example 154		^{1}H-NMR(δppm, DMSO-d_6) 0.96-1.30 (4H, m), 1.50-1.82 (9H, m), 1.91-2.33 (4H, m), 2.01 (2H, t, J=7.6Hz), 2.51 (2H, t, J=7.7Hz), 2.86 (1.74H, s), 2.96 (1.26H, s), 3.33-3.46 (1H, m), 4.08-4.16 (0.42H, m), 4.22-4.31 (0.58H, m), 4.46-4.57 (0.58H, m), 4.67-4.78 (0.42H, m), 7.10-7.18 (3H, m), 7.21-7.28 (2H, m), 7.62-7.69 (1H, m), 8.08 (3H, brs).
Example 155		^{1}H-NMR(δppm, DMSO-d_6) 0.97-1.32 (4H, m), 1.50-1.71 (5H, m), 1.74-1.86 (2H, m), 1.92-2.33 (4H, m), 2.87 (1.74H, s), 2.96 (1.26H, s), 3.05 (2H, s), 3.33-3.45 (1H, m), 4.09-4.16 (0.42H, m), 4.22-4.31 (0.58H, m), 4.45-4.56 (0.58H, m), 4.68-4.79 (0.42H, m), 7.91-7.98 (1H, m), 8.07 (3H, brs), 12.25 (1H, brs).
Example 156		^{1}H-NMR(δppm, DMSO-d_6) 0.95-1.30 (4H, m), 1.49-1.70 (5H, m), 1.70-1.83 (2H, m), 1.91-2.32 (4H, m), 2.24 (2H, t, J=7.0Hz), 2.37 (2H, t, J=7.0Hz), 2.86 (1.74H, s), 2.96 (1.26H, s), 3.31-3.43 (1H, m), 4.07-4.16 (0.42H, m), 4.22-4.31 (0.58H, m), 4.45-4.56 (0.58H, m), 4.68-4.79 (0.42H, m), 7.66-7.75 (1H, m), 8.05 (3H, brs).
Example 157		^{1}H-NMR(δppm, DMSO-d_6) 0.95-1.30 (4H, m), 1.50-1.83 (9H, m), 1.91-2.35 (4H, m), 2.02 (2H, t, J=7.3Hz), 2.16 (2H, t, J=7.4Hz), 2.86 (1.74H, s), 2.96 (1.26H, s), 3.30-3.42 (1H, m), 4.08-4.16 (0.42H, m), 4.23-4.31 (0.58H, m), 4.45-4.57 (0.58H, m), 4.68-4.79 (0.42H, m), 7.62-7.71 (1H, m), 8.06 (3H, brs).

Table 1-41

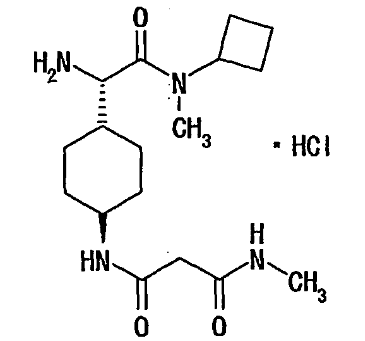
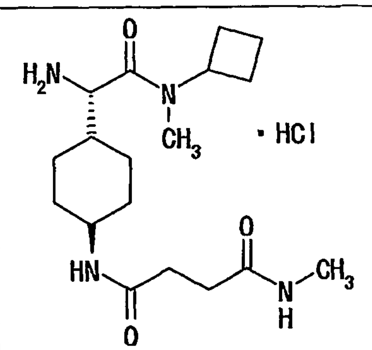
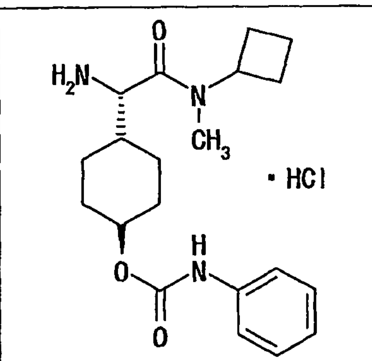
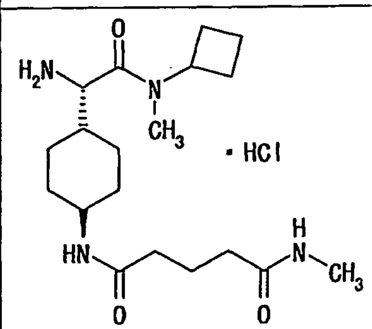
Example 158		^{1}H-NMR(δppm, DMSO-d$_6$) 0.96-1.31 (4H, m), 1.50-1.72 (5H, m), 1.72-1.84 (2H, m), 1.91-2.33 (4H, m), 2.55 (3H, d, J=4.6Hz), 2.87 (1.74H, s), 2.94 (2H, s), 2.96 (1.26H, s), 3.32-3.44 (1H, m), 4.08-4.16 (0.42H, m), 4.23-4.31 (0.58H, m), 4.45-4.56 (0.58H, m), 4.68-4.78 (0.42H, m), 7.85-7.95 (2H, m), 8.08 (3H, brs).
Example 159		^{1}H-NMR(δppm, DMSO-d$_6$) 0.95-1.31 (4H, m), 1.49-1.70 (5H, m), 1.70-1.81 (2H, m), 1.92-2.33 (4H, m), 2.23 (4H, s), 2.51 (3H, d, J=4.4Hz), 2.86 (1.74H, s), 2.96 (1.26H, s), 3.30-3.43 (1H, m), 4.07-4.16 (0.42H, m), 4.22-4.31 (0.58H, m), 4.45-4.57 (0.58H, m), 4.67-4.79 (0.42H, m), 7.64-7.76 (2H, m), 8.07 (3H, brs).
Example 160		^{1}H-NMR(δppm, DMSO-d$_6$) 1.18-1.42 (4H, m), 1.54-1.79 (5H, m), 1.92-2.33 (6H, m), 2.87 (1.74H, s), 2.98 (1.26H, s), 4.16 (0.42H, d, J=5.1Hz), 4.30 (0.58H, d, J=5.1Hz), 4.41-4.58 (1.58H, m), 4.68-4.80 (0.42H, m), 6.94 (1H, dd, J=7.4, 7.4Hz), 7.23 (2H, dd, J=8.1, 7.4Hz), 7.35 (2H, d, J=8.1Jz), 8.09 (3H, brs), 9.54 (1H, s).
Example 161		^{1}H-NMR(δppm, DMSO-d$_6$) 0.96-1.30 (4H, m), 1.50-1.82 (9H, m), 1.91-2.33 (8H, m), 2.52 (3H, d, J=4.6Hz), 2.86 (1.74H, s), 2.96 (1.26H, s), 3.32-3.45 (1H, m), 4.08-4.16 (0.42H, m), 4.23-4.31 (0.58H, m), 4.45-4.56 (0.58H, m), 4.67-4.78 (0.42H, m), 7.59-7.73 (2H, m), 8.08 (3H, brs).

Table 1-42

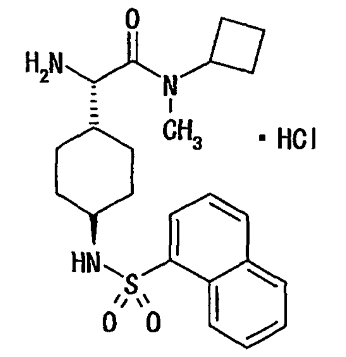
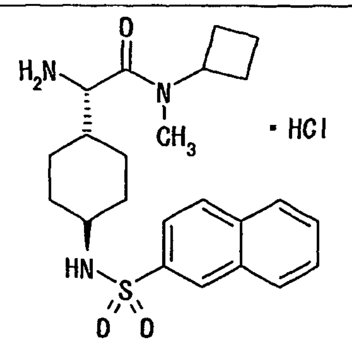
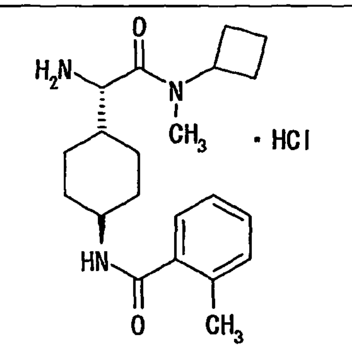
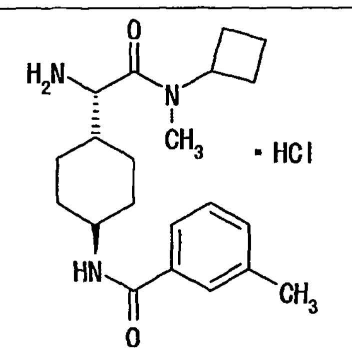
Example 162		^{1}H-NMR(δppm, DMSO-d_6) 0.87-1.12 (4H, m), 1.35-1.64 (7H, m), 1.86-2.27 (4H, m), 2.74-2.86 (1H, m), 2.80 (1.74H, s), 2.87 (1.26H, s), 3.99 (0.42H, d, J=5.6Hz), 4.14 (0.58H, d, J=5.6Hz), 4.34-4.45 (0.58H, m), 4.60-4.71 (0.42H, m), 7.57-7.71 (3H, m), 7.92-8.01 (1H, m), 7.97 (3H, brs), 8.06, (1H, d, J=7.4Hz), 8.12 (1H, d, J=7.2Hz), 8.19 (1H, d, J=8.1Hz), 8.60 (1H, d, J=8.1Hz).
Example 163		^{1}H-NMR(δppm, DMSO-d_6) 0.89-1.18 (4H, m), 1.38-1.68 (7H, m), 1.87-2.27 (4H, m), 2.75-2.86 (1H, m), 2.81 (1.74H, s), 2.88 (1.26H, s), 4.00 (0.42H, d, J=5.6Hz), 4.15 (0.58H, d, J=5.6Hz), 4.35-4.46 (0.58H, m), 4.62-4.72 (0.42H, m), 7.60-7.71 (2H, m), 7.74-7.83 (2H, m), 7.93 (3H, brs), 8.01, (1H, d, J=7.7Hz), 8.07-8.16 (2H, m), 8.41 (1H, s).
Example 164		^{1}H-NMR(δppm, DMSO-d_6) 1.11-1.38 (4H, m), 1.52-1.74 (5H, m), 1.81-2.36 (6H, m), 2.28 (3H, s), 2.88 (1.74H, s), 2.97 (1.26H, s), 3.55-3.69 (1H, m), 4.10-4.20 (0.42H, m), 4.24-4.35 (0.58H, m), 4.47-4.59 (0.58H, m), 4.68-4.81 (0.42H, m), 7.13-7.31 (4H, m), 8.00-8.18 (4H, m).
Example 165		^{1}H-NMR(δppm, DMSO-d_6) 1.14-1.38 (4H, m), 1.53-1.75 (5H, m), 1.78-1.92 (2H, m), 1.93-2.36 (4H, m), 2.32 (3H, s), 2.88 (1.74H, s), 2.98 (1.26H, s), 3.60-3.74 (1H, m), 4.10-4.19 (0.42H, m), 4.25-4.35 (0.58H, m), 4.48-4.60 (0.58H, m), 4.69-4.81 (0.42H, m), 7.23-7.33 (2H, m), 7.53-7.64 (2H, m), 8.01-8.22 (4H, m).

Table 1-43

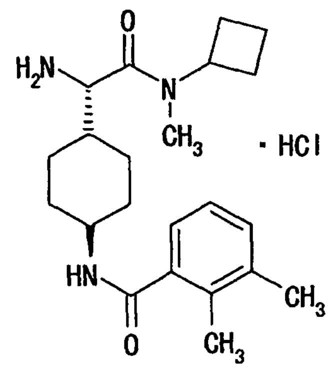
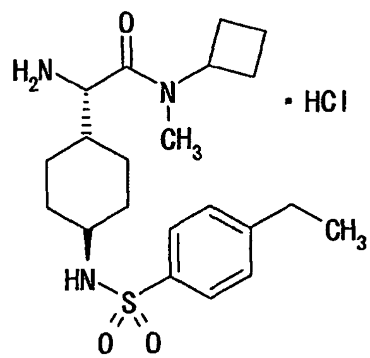
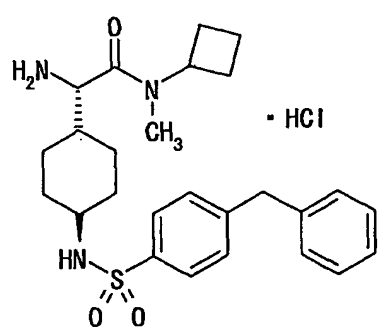
Example 166		^{1}H-NMR(δppm, DMSO-d_6) 1.10-1.34 (4H, m), 1.52-1.72 (5H, m), 1.82-1.92 (2H, m), 1.93-2.34 (4H, m), 2.14 (3H, s), 2.22 (3H, s), 2.88 (1.74H, s), 2.97 (1.26H, s), 3.54-3.68 (1H, m), 4.11-4.19 (0.42H, m), 4.26-4.34 (0.58H, m), 4.47-4.58 (0.58H, m), 4.68-4.80 (0.42H, m), 7.01 (1H, d, J=7.5Hz), 7.06 (1H, dd, J=7.5, 7.2Hz), 7.16 (1H, d, J=7.2Hz), 7.99-8.18 (4H, m).
Example 167		^{1}H-NMR(δppm, DMSO-d_6) 0.93-1.24 (4H, m), 1.17 (3H, t, J=7.6Hz), 1.40-1.68 (7H, m), 1.88-2.32 (4H, m), 2.66 (2H, q, J=7.6Hz), 2.71-2.86 (1H, m), 2.82 (1.74H, s), 2.90 (1.26H, s), 4.03 (0.42H, d, J=5.6Hz), 4.17 (0.58H, d, J=5.6Hz), 4.38-4.49 (0.58H, m), 4.63-4.75 (0.42H, m), 7.38 (2H, d, J=8.2Hz), 7.55-7.63 (1H, m), 7.67 (2H, d, J=8.2Hz), 7.97 (3H, brs).
Example 168		^{1}H-NMR(δppm, DMSO-d_6) 0.94-1.15 (4H, m), 1.40-1.68 (7H, m), 1.90-2.29 (4H, m), 2.68-2.81 (1H, m), 2.83 (1.74H, s), 2.90 (1.26H, s), 3.98-4.07 (0.42H, m), 4.01 (2H, s), 4.13-4.21 (0.58H, m), 4.37-4.48 (0.58H, m), 4.63-4.75 (0.42H, m), 7.14-7.31 (5H, m), 7.40 (2H, d, J=8.3Hz), 7.56-7.64 (1H, m), 7.68 (2H, d, J=8.3Hz), 8.00 (3H, brs).

Table 1-44

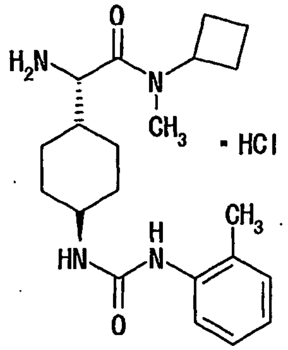
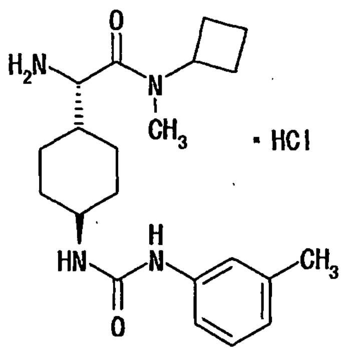
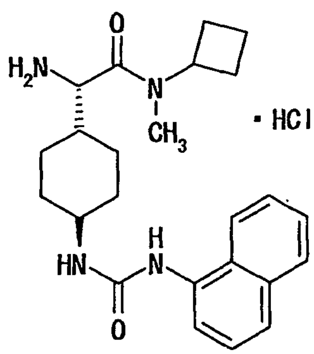
Example 169		^{1}H-NMR(δppm, DMSO-d_6) 0.96-1.36 (m, 4H), 1.54-1.75 (m, 5H), 1.85-2.33 (m, 6H), 2.14 (s, 3H), 2.88 (s, 1.74H), 2.97 (s, 1.26H), 3.23-3.36 (m, 1H), 4.10-4.19 (m, 0.42H), 4.25-4.33 (m, 0.58H), 4.47-4.58 (m, 0.58H), 4.69-4.80 (m, 0.42H), 6.66 (bs, 1H), 6.80 (dd, 1H, J=7.4, 7.4Hz), 6.99-7.09 (m, 2H), 7.63 (bs, 1H), 7.79 (d, 1H, J=8.4Hz), 8.07 (bs, 3H).
Example 170		^{1}H-NMR(δppm, DMSO-d_6) 0.96-1.36 (4H, m), 1.52-1.76 (5H, m), 1.81-2.34 (6H, m), 2.20 (3H, s), 2.87 (1.74H, s), 2.97 (1.26H, s), 3.22-3.36 (1H, m), 4.11-4.20 (0.42H, m), 4.25-4.34 (0.58H, m), 4.46-4.57 (0:58H, m), 4.69-4.80 (0.42H, m), 6.11-6.23 (1H, m), 6.65 (1H, d, J=7.7Hz), 7.04 (1H, d, J=7.7, 7.7Hz), 7.12 (1H, d, J=7.7Hz), 7.16 (1H, s), 8.05 (3H, brs), 8.43 (1H, s).
Example 171		^{1}H-NMR(δppm, DMSO-d_6) 1.00-1.39 (4H, m), 1.54-1.78 (5H, m), 1.90-2.34 (6H, m), 2.88 (1.74H, s), 2.98 (1.26H, s), 3.30-3.44 (1H, m), 4.12-4.20 (0.42H, m), 4.27-4.35 (0.58H, m), 4.48-4.58 (0.58H, m), 4.70-4.81 (0.42H, m), 6.84 (1H, brs), 7.36 (1H, dd, J=7.9, 7.9Hz), 7.43-7.53 (3H, m), 7.80-7.88 (1H, m), 7.98 (1H, d, J=7.7Hz), 8.07 (3H, brs), 8.15 (1H, d, J=7.7Hz), 8.61 (1H, s).

Table 1-45

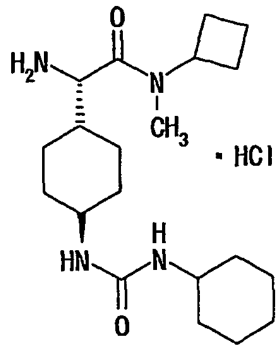
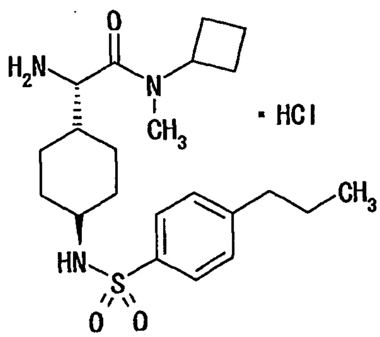
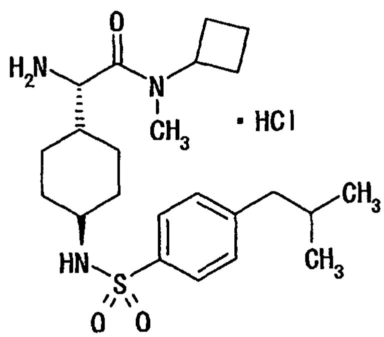
Example 172		^{1}H-NMR(δppm, DMSO-d_6) 0.86-1.30 (m, 9H), 1.42-1.73 (m, 10H), 1.74-1.87 (m, 2H), 1.92-2.34 (m, 4H), 2.86 (s, 1.74H), 2.96 (s, 1.26H), 3.12-3.24 (m, 1H), 3.24-3.34 (m, 1H), 4.06-4.15 (m, 0.42H), 4.21-4.31 (m, 0.58H), 4.44-4.56 (m, 0.58H), 4.66-4.80 (m, 0.42H), 5.56 (bs, 2H), 8.06 (bs, 3H).
Example 173		^{1}H-NMR(δppm, DMSO-d_6) 0.86 (3H, t, J=7.3Hz), 0.95-1.14 (4H, m), 1.41-1.66 (9H, m), 1.89-2.28 (4H, m), 2.61 (2H, t, J=7.2Hz), 2.69-2.80 (1H, m), 2.83 (1.74H, s), 2.90 (1.26H, s), 4.04 (0.42H, d, J=5.6Hz), 4.17 (0.58H, d, J=5.6Hz), 4.38-4.49 (0.58H, m), 4.63-4.74 (0.42H, m), 7.36 (2H, d, J=8.3Hz), 7.54-7.62 (1H, m), 7.67 (2H, d, J=8.3Hz), 7.98 (3H, brs).
Example 174		^{1}H-NMR(δppm, DMSO-d_6) 0.83 (6H, d, J=6.7Hz), 0.89-1.14 (4H, m), 1.38-1.66 (7H, m), 1.78-2.29 (5H, m), 2.50 (2H, t, J=7.6Hz), 2.69-2.80 (1H, m), 2.82 (1.74H, s), 2.90 (1.26H, s), 4.03 (0.42H, d, J=5.3Hz), 4.17 (0.58H, d, J=5.3Hz), 4.37-4.49 (0.58H, m), 4.63-4.74 (0.42H, m), 7.33 (2H, d, J=8.1Hz), 7.53-7.61 (1H, m), 7.67 (2H, d, J=8.1Hz), 7.97 (3H, brs).

Table 1-46

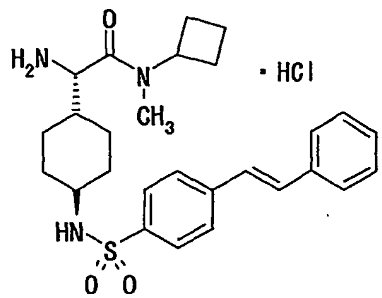
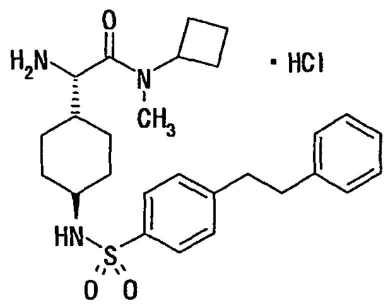
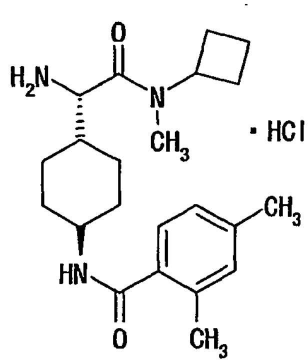
Example 175		^{1}H-NMR(δppm, DMSO-d_6) 0.98-1.19 (4H, m), 1.43-1.73 (7H, m), 1.91-2.31 (4H, m), 2.77-2.88 (1H, m), 2.85 (1.74H, s), 2.93 (1.26H, s), 4.02-4.11 (0.42H, m), 4.16-4.25 (0.58H, m), 4.39-4.51 (0.58H, m), 4.65-4.77 (0.42H, m), 7.28-7.36 (2H, m), 7.37-7.46 (3H, m), 7.60-7.73 (3H, m), 7.74-7.82 (4H, m), 8.02 (3H, brs).
Example 176		^{1}H-NMR(δppm, DMSO-d_6) 0.96-1.19 (4H, m), 1.42-1.69 (7H, m), 1.91-2.32 (4H, m), 2.70-2.83 (1H, m), 2.83-2.99 (4H, m), 2.85 (1.74H, s), 2.93 (1.26H, s), 4.06 (0.42H, d, J=5.6Hz), 4.21 (0.58H, d, J=5.6Hz), 4.41-4.52 (0.58H, m), 4.67-4.77 (0.42H, m), 7.12-7.19 (3H, m), 7.20-7.28 (2H, m), 7.38 (2H, d, J=8.2Hz), 7.57-7.63 (1H, m), 7.67 (2H, d, J=8.2Hz), 8.02 (3H, brs)
Example 177		^{1}H-NMR(δppm, DMSO-d_6) 1.12-1.38 (4H, m), 1.55-1.75 (5H, m), 1.83-1.94 (2H, m), 1.96-2.37 (4H, m), 2.27 (6H, s), 2.90 (1.74H, s), 2.99 (1.26H, s), 3.55-3.69 (1H, m), 4.13-4.21 (0.42H, m), 4.27-4.37 (0.58H, m), 4.50-4.61 (0.58H, m), 4.71-4.81 (0.42H, m), 6.96-7.04 (2H, m), 7.15 (1H, d, J= 7.6Hz), 7.94-8.03 (1H, m), 8.12 (3H, brs).

Table 1-47

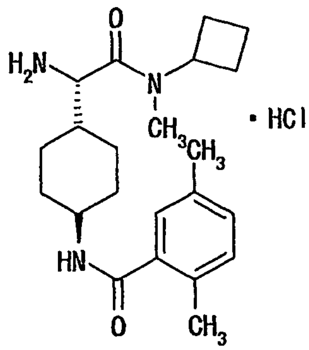
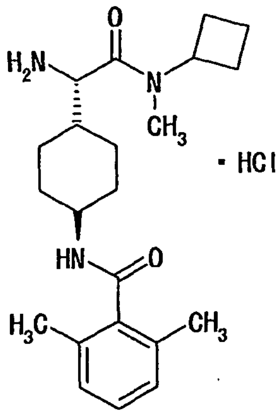
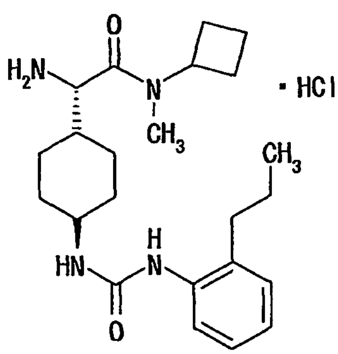
Example 178		^{1}H-NMR(δppm, DMSO-d_6) 1.13-1.38 (4H, m), 1.54-1.75 (5H, m), 1.83-1.94 (2H, m), 1.97-2.36 (4H, m), 2.24 (3H, s), 2.26 (3H, s), 2.90 (1.74H, s), 2.99 (1.26H, s), 3.55-3.69 (1H, m), 4.12-4.22 (0.42H, m), 4.27-4.37 (0.58H, m), 4.49-4.61 (0.58H, m), 4.70-4.82 (0.42H, m), 7.02-7.23 (3H, m), 7.99-8.22 (4H, m).
Example 179		^{1}H-NMR(δppm, DMSO-d_6) 1.11-1.40 (4H, m), 1.54-1.75 (5H, m), 1.84-1.95 (2H, m), 1.95-2.37 (4H, m), 2.19 (6H, s), 2.89 (1.74H, s), 2.99 (1.26H, s), 3.60-3.73 (1H, m), 4.13-4.22 (0.42H, m), 4.28-4.36 (0.58H, m), 4.49-4.61 (0.58H, m), 4.69-4.81 (0.42H, m), 7.01 (2H, d, J=7.6Hz), 7.15 (1H, dd, J= 7.6, 7.6Hz), 8.03-8.22 (4H, m).
Example 180		^{1}H-NMR(δppm, DMSO-d_6) 0.91 (3H, t, J=7.3Hz), 0.99-1.38 (4H, m), 1.44-1.78 (7H, m), 1.86-2.38 (6H, m), 2.51 (2H, t, J=7.2Hz), 2.90 (1.74H, s), 3.00 (1.26H, s), 3.25-3.38 (1H, m), 4.12-4.21 (0.42H, m), 4.27-4.36 (0.58H, m), 4.49-4.60 (0.58H, m), 4.72-4.82 (0.42H, m), 6.61-6.76 (1H, m), 6.87 (1H, dd, J=7.4, 7.4Hz), 7.01-7.10 (2H, m), 7.58-7.65 (1H, m), 7.76 (1H, d, J=8.2Hz), 8.10 (3H, brs).

Table 1-48

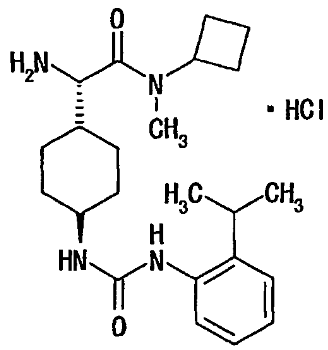
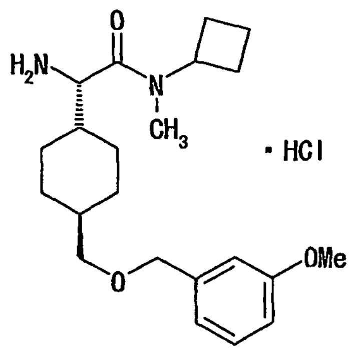
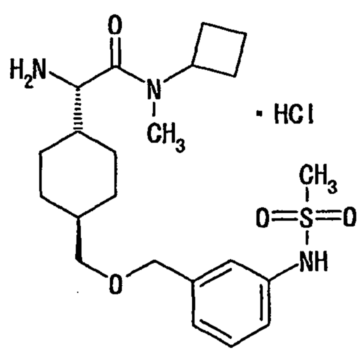
Example 181		^{1}H-NMR(δppm, DMSO-d_6) 0.98-1.37 (4H, m), 1.14 (6H, d, J=.7Hz), 1.55-1.78 (5H, m), 1.87-2.37 (6H, m), 2.90 (1.74H, s), 2.99 (1.26H, s), 3.05-3.15 (1H, m), 3.25-3.38 (1H, m), 4.12-4.21 (0.42H, m), 4.27-4.36 (0.58H, m), 4.48-4.60 (0.58H, m), 4.70-4.83 (0.42H, m), 6.57 (1H, brs), 6.95 (1H, dd, J=8.1, 7.9Hz), 7.05 (1H, dd, J=7.9, 7.4Hz), 7.19 (1H, d, J=7.4Hz), 7.58-7.72 (2H, m), 8.10 (3H, brs).
Example 182		^{1}H-NMR(δppm, $CDCl_3$) 0.87-1.30 (4H, m), 1.35-1.79 (7H, m), 1.79-1.94 (3H, m), 2.02-2.20 (3H, m), 2.20-2.34 (1H, m), 2.94 (1.74H, s), 2.95 (1.26H, s), 3.26 (2H, d, J=6.5Hz), 3.41-3.45 (0.42H, m), 3.50-3.55 (0.58H, m), 3.80 (3H, s), 4.32-4.43 (0.58H, m), 4.46 (2H, s), 4.85-4.98 (0.42H, m), 6.78-6.83 (1H, m), 6.86-6.92 (2H, m), 7.24 (1H, dd, J=8.3, 7.9Hz).
Example 183		^{1}H-NMR(δppm, DMSO-d_6) 0.81-1.01 (2H, m), 1.01-1.53 (3H, m), 1.53-1.73 (5H, m), 1.74-1.84 (2H, m), 1.93-2.35 (4H, m), 2.88 (1.74H, s), 2.96 (3H, s), 2.98 (1.26H, s), 3.22 (2H, d, J=6.5Hz), 4.08-4.15 (0.42H, m), 4.20-4.30 (0.58H, m), 4.40 (2H, s), 4.45-4.56 (0.58H, m), 4.69-4.79 (0.42H, m), 7.01 (1H, d, J=7.7Hz), 7.11 (1H, d, J=7.5Hz), 7.17 (1H, s), 7.28 (1H, dd, J=7.7, 7,5Hz), 8.07 (3H, brs), 9.75 (1H, s).

Table 1-49

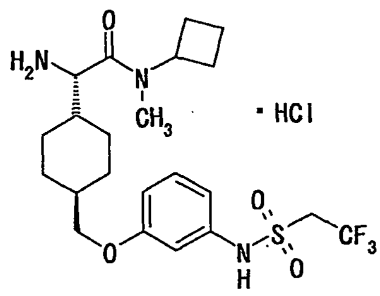
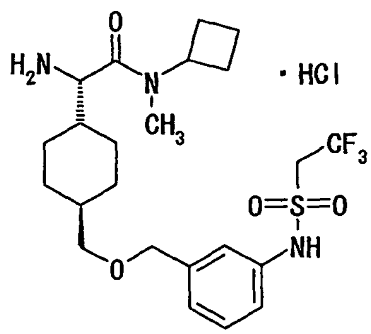
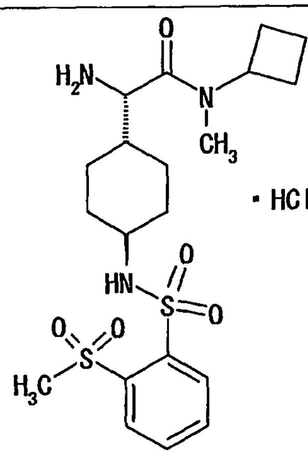
Example 184		^{1}H-NMR(δppm, DMSO-d_6) 0.92-1.31 (4H, m), 1.31-1.77 (6H, m), 1.82-1.93 (2H, m), 1.94-2.36 (4H, m), 2.89 (1.74H, s), 2.99 (1.26H, s), 3.74 (2H, d, J=6.0Hz), 4.14-4.18 (0.42H, m), 4.28-4.33 (0.58H, m), 4.45-4.59 (2.58H, m), 4.72-4.83 (0.42H, m), 6.69 (1H, d, J=7.9Hz), 6.74-6.80 (2H, m), 7.22 (1H, dd, J=8.2, 7,9Hz), 8.14 (3H, bs).
Example 185		^{1}H-NMR(δppm, DMSO-d_6) 0.80-1.03 (2H, m), 1.03-1.53 (3H, m), 1.53-1.72 (5H, m), 1.74-1.84 (2H, m), 1.93-2.35 (4H, m), 2.88 (1.74H, s), 2.97 (1.26H, s), 3.22 (2H, d, J=6.2Hz), 4.11-4.17 (0.42H, m), 4.26-4.31 (0.58H, m), 4.36-4.58 (2.58H, m), 4.41 (2H, s), 4.70-4.83 (0.42H, m), 7.05 (1H, d, J=7.7Hz), 7.11 (1H, d, J=7.9Hz), 7.18 (1H, s), 7.30 (1H, dd, J=7.9, 7,7Hz), 8.15 (3H, brs).
Example 186		^{1}H-NMR(δppm, DMSO-d_6) 0.96-1.28 (4H, m), 1.44-1.70 (7H, m), 1.89-2.35 (4H, m), 2.84 (1.74H, s), 2.89-3.04 (1H, m), 2.92 (1.26H, s), 3.45 (3H, s), 4.03-4.09 (0.42H, m), 4.18-4.24 (0.58H, m), 4.39-4.51 (0.58H, m), 4.65-4.77 (0.42H, m), 6.76 (1H, brs), 7.87-8.09 (5H, m), 8.13-8.27 (2H, m).

Table 1-50

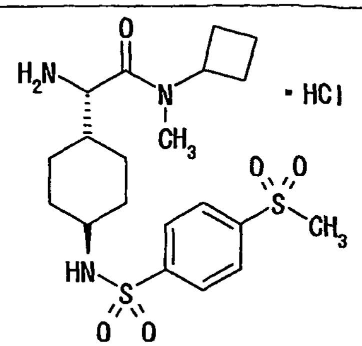
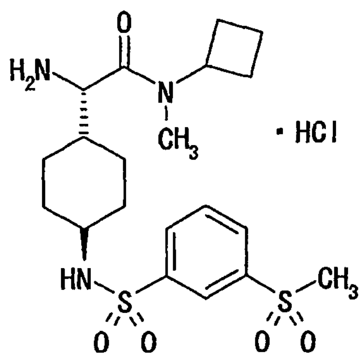
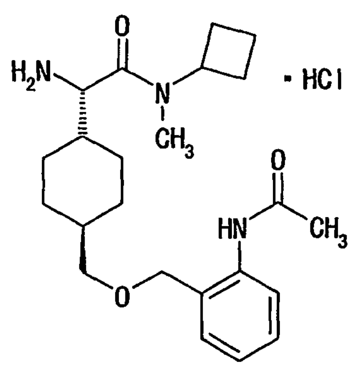
Example 187		^{1}H-NMR(δppm, DMSO-d_6) 0.98-1.25 (4H, m), 1.45-1.74 (7H, m), 1.91-2.34 (4H, m), 2.83-2.96 (1H, m), 2.85 (1.74H, s), 2.93 (1.26H, s), 3.33 (3H, s), 4.03-4.09 (0.42H, m), 4.18-4.24 (0.58H, m), 4.41-4.52 (0.58H, m), 4.66-4.77 (0.42H, m), 7.97-8.10 (6H, m), 8.11-8.27 (2H, m).
Example 188		^{1}H-NMR(δppm, DMSO-d_6) 1.00-1.25 (4H, m), 1.44-1.70 (7H, m), 1.92-2.31 (4H, m), 2.81-2.96 (1H, m), 2.85 (1.74H, s), 2.93 (1.26H, s), 3.32 (3H, s), 4.02-4.10 (0.42H, m), 4.16-4.25 (0.58H, m), 4.41-4.52 (0.58H, m), 4.66-4.76 (0.42H, m), 7.89 (1H, dd, J=7.9, 7.9Hz), 7.97-8.10 (4H, m), 8.13 (1H, d, J=7.9Hz), 8.19 (1H, d, J=7.9Hz), 8.29 (1H, s).
Example 189		^{1}H-NMR(δppm, DMSO-d_6) 0.98-1.29 (4H, m), 1.29-1.86 (8H, m), 1.93-2.37 (4H, m), 2.04 (3H, s), 2.88 (1.74H, s), 2.97 (1.26H, s), 3.22 (2H, d, J=5.5Hz), 4.09-4.19 (0.42H, m), 4.24-4.34 (0.58H, m), 4.43 (2H, s), 4.48-4.58 (0.58H, m), 4.70-4.83 (0.42H, m), 7.14 (1H, dd, J=7.4, 6.7Hz), 7.24 (1H, dd, J=7.9, 6.7Hz), 7.34 (1H, d, J=7.4Hz), 7.46 (1H, d, J=7.9Hz), 8.07 (3H, brs), 9.28 (1H, brs).

Table 1-51

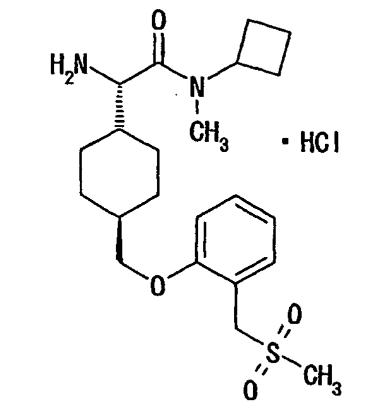
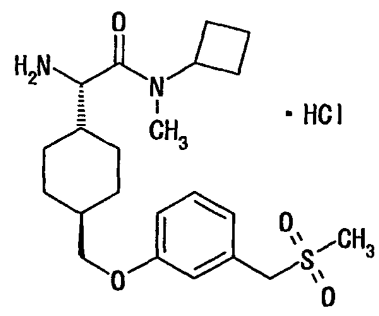
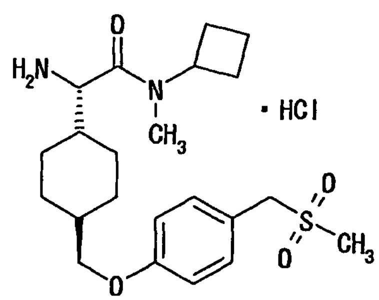
Example 190		^{1}H-NMR(δppm, DMSO-d_6) 1.00-1.29 (4H, m), 1.56-1.77 (6H, m), 1.86-1.95 (2H, m), 1.96-2.35 (4H, m), 2.84 (3H, s), 2.90 (1.74H, s), 3.00 (1.26H, s), 3.82 (2H, d, J=5.8Hz), 4.16 (0.42H, d, J=5.5Hz), 4.31 (0.58H, d, J=5.5Hz), 4.41 (2H, s), 4.50-4.60 (0.58H, m), 4.73-4.83 (0.42H, m), 6.95 (1H, dd, J=7.4, 7.2Hz), 7.03 (1H, d, J=8.1Hz), 7.29-7.37 (2H, m), 8.06 (3H, brs).
Example 191		^{1}H-NMR(δppm, DMSO-d_6) 0.96-1.29 (4H, m), 1.57-1.77 (6H, m), 1.83-1.94 (2H, m), 1.95-2.35 (4H, m), 2.88 (3H, s), 2.89 (1.74H, s), 2.99 (1.26H, s), 3.77 (2H, d, J=6.2Hz), 4.16 (0.42H, d, J=4.9Hz), 4.31 (0.58H, d, J=4.9Hz), 4.43 (2H, s), 4.49-4.59 (0.58H, m), 4.72-4.83 (0.42H, m), 6.89-7.00 (3H, m), 7.28 (1H, dd, J=8.1, 7.9Hz), 8.06 (3H, brs).
Example 192		^{1}H-NMR(δppm, DMSO-d_6) 0.94-1.30 (4H, m), 1.55-1.75 (6H, m), 1.82-1.94 (2H, m), 1.95-2.35 (4H, m), 2.85 (3H, s), 2.89 (1.74H, s), 2.99 (1.26H, s), 3.77 (2H, d, J=6.3Hz), 4.16 (0.42H, d, J=5.1Hz), 4.30 (0.58H, d, J=5.1Hz), 4.37 (2H, s), 4.49-4.59 (0.58H, m), 4.72-4.82 (0.42H, m), 6.92 (2H, d, J=8.6Hz), 7.29 (2H, d, J=8.6Hz), 8.06 (3H, brs).

Table 1-52

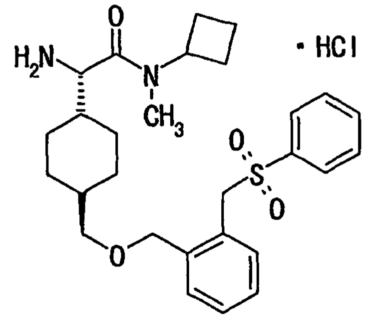
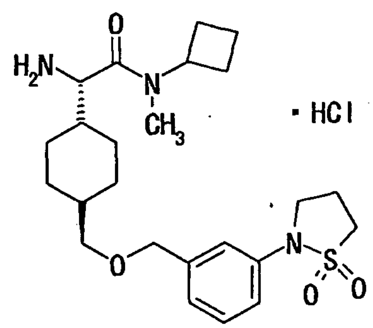
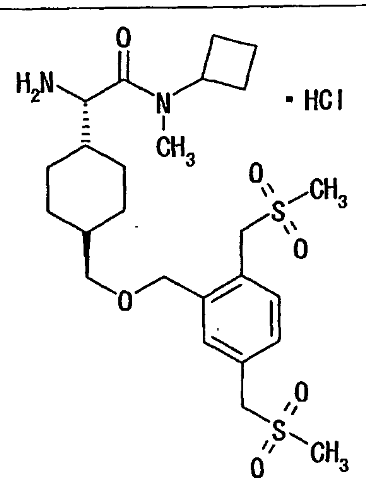
Example 193		^{1}H-NMR(δppm, DMSO-d_6) 0.81-0.96 (2H, m), 1.02-1.51 (3H, m), 1.51-1.71 (7H, m), 1.95-2.36 (4H, m), 2.88 (1.74H, s), 2.97 (1.26H, s), 3.16 (2H, d, J=6.3Hz), 4.14 (0.42H, d, J=5.3Hz), 4.29 (0.58H, d, J=5.3Hz), 4.36 (2H, s), 4.46-4.58 (0.58H, m), 4.71 (2H, s), 4.72-4.82 (0.42H, m), 7.06 (1H, d, J=7.4Hz), 7.17-7.24 (1H, m), 7.27-7.36 (2H, m), 7.56-7.65 (2H, m), 7.67-7.77 (3H, m), 8.03 (3H, bs).
Example 194		^{1}H-NMR(δppm, DMSO-d_6) 0.82-1.00 (2H, m), 1.03-1.52 (3H, m), 1.52-1.71 (5H, m), 1.73-1.85 (2H, m), 1.95-2.45 (6H, m), 2.89 (1.74H, s), 2.98 (1.26H, s), 3.23 (2H, d, J=6.3Hz), 3.51 (2H, t, J=7.4Hz), 3.73 (2H, t, J=6.7Hz), 4.11-4.19 (0.42H, m), 4.26-4.33 (0.58H, m), 4.43 (2H, s), 4.48-4.58 (0.58H, m), 4.71-4.83 (0.42H, m), 7.03 (1H, d, J=7.9Hz), 7.09 (1H, d, J=7.8Hz), 7.17 (1H, s), 7.34 (1H, dd, J=7.9, 7.8Hz), 8.07 (3H, brs).
Example 195		^{1}H-NMR(δppm, DMSO-d_6) 0.80-1.29 (4H, m), 1.42-1.85 (8H, m), 1.93-2.35 (4H, m), 2.89 (1.74H, s), 2.93 (3H, s), 2.98 (1.26H, s), 3.00 (3H, s), 3.26 (2H, d, J=6.2Hz), 4.13-4.17 (0.42H, m), 4.27-4.32 (0.58H, m), 4.44-4.56 (0.58H, m), 4.53 (2H, s), 4.58 (2H, s), 4.61 (2H, s), 4.72-4.83 (0.42H, m), 7.36 (1H, d, J=7.7Hz), 7.43 (1H, d, J=7.7Hz), 7.46 (1H, s), 8.05 (3H, brs).

Table 1-53

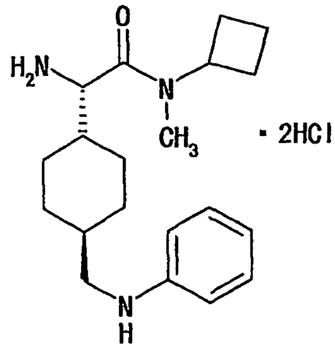
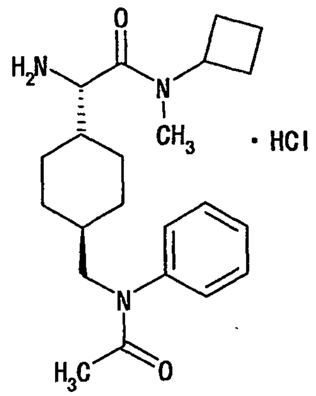
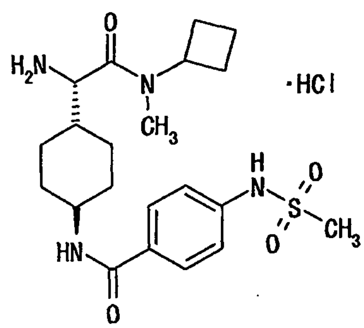
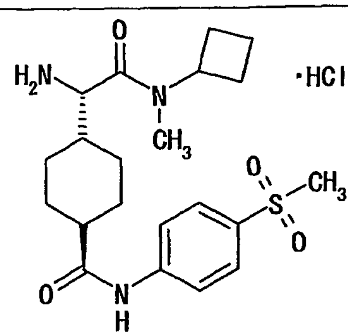
Example 196		^{1}H-NMR(δppm, DMSO-d_6) 0.80-1.28 (4H, m), 1.49-1.75 (6H, m), 1.83-2.36 (6H, m), 2.89 (1.74H, s), 2.93-3.02 (2H ,m), 2.98 (1.26H, s), 4.10-4.19 (0.42H, m), 4.25-4.34 (0.58H, m), 4.48-4.59 (0.58H, m), 4.71-4.83 (0.42H, m), 6.75-7.39 (5H, m), 8.10 (3H, brs).
Example 197		^{1}H-NMR(δppm, DMSO-d_6) 0.75-1.31 (5H, m), 1.51-1.79 (7H, m), 1.73 (3H, s), 1.92-2.34 (4H, m), 2.87 (1.74H, s), 2.96 (1.26H, s), 3.50 (2H, d, J=7.0Hz), 4.06-4.15 (0.42H, m), 4.21-4.31 (0.58H, m), 4.44-4.56 (0.58H, m), 4.69-4.81 (0.42H, m), 7.26-7.39 (3H, m), 7.41-7.50 (2H, m), 8.05 (3H, brs).
Example 198		^{1}H-NMR(δppm, DMSO-d_6) 1.14-1.39 (4H, m), 1.55-1.76 (5H, m), 1.81-1.93 (2H, m), 1.95-2.39 (4H, m), 2.91 (1.74H, s), 3.01 (1.26H, s), 3.04 (3H, s), 3.61-3.75 (1H, m), 4.14-4.23 (0.42H, m), 4.29-4.38 (0.58H, m), 4.51-4.63 (0.58H, m), 4.73-4.84 (0.42H, m), 7.23 (2H, d, J=8.8Hz), 7.41 (2H, d, J=8.8Hz), 8.05-8.22 (4H, m), 10.11 (1H, brs).
Example 199		^{1}H-NMR(δppm, DMSO-d_6) 1.11-1.49 (4H, m), 1.56-1.83 (5H, m), 1.86-2.40 (7H, m), 2.91 (1.74H, s), 3.01 (1.26H, s), 3.15 (3H, s), 4.18-4.24 (0.42H, m), 4.33-4.39 (0.58H, m), 4.51-4.63 (0.58H, m), 4.72-4.84 (0.42H, m), 7.79-7.90 (4H, m), 8.12 (3H, brs), 10.46 (1H, brs).

Table 1-54

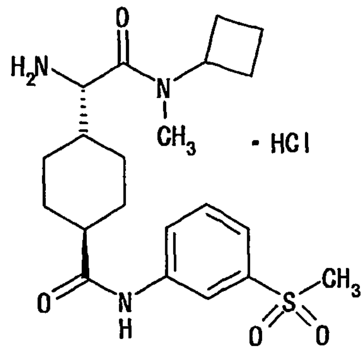
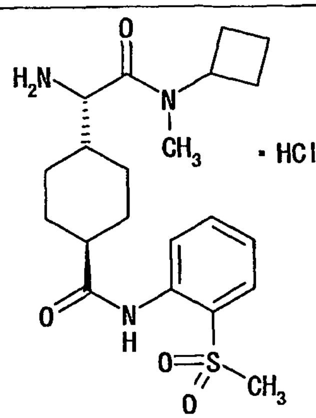
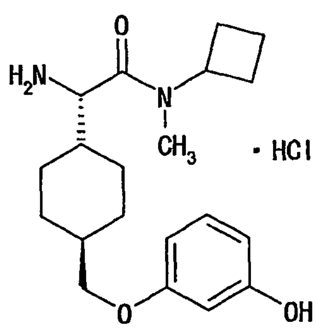
Example 200		^{1}H-NMR(δppm, DMSO-d_6) 1.12-1.51 (4H, m), 1.57-1.82 (5H, m), 1.86-2.37 (7H, m), 2.91 (1.74H, s), 3.01 (1.26H, s), 3.18 (3H, s), 4.18-4.24 (0.42H, m), 4.33-4.39 (0.58H, m), 4.51-4.63 (0.58H, m), 4.72-4.84 (0.42H, m), 7.53-7.61 (2H, m), 7.82-7.90 (1H, m), 8.12 (3H, brs), 8.29 (1H, s), 10.38 (1H, brs).
Example 201		^{1}H-NMR(δppm, DMSO-d_6) 1.12-1.48 (4H, m), 1.56-1.83 (5H, m), 1.95-2.38 (7H, m), 2.91 (1.74H, s), 3.01 (1.26H, s), 3.25 (3H, s), 4.17-4.22 (0.42H, m), 4.32-4.38 (0.58H, m), 4.50-4.62 (0.58H, m), 4.73-4.84 (0.42H, m), 7.41 (1H, dd, J=7.9, 7.5Hz), 7.72 (1H, dd, J=8.2, 7.5Hz), 7.90 (1H, d, J=7.9Hz), 8.01 (1H, d, J=8.2Hz), 8.09 (3H, brs), 9.63 (1H, brs).
Example 202		^{1}H-NMR(δppm, DMSO-d_6) 0.90-1.33 (4H, m), 1.53-1.77 (6H, m), 1.80-1.93 (2H, m), 1.95-2.37 (4H, m), 2.90 (1.74H, s), 2.99 (1.26H, s), 3.69 (2H, d, J=6.3Hz), 4.16 (0.42H, d, J=5.3Hz), 4.31 (0.58H, d, J=5.3Hz), 4.49-4.60 (0.58H, m), 4.72-4.84 (0.42H, m), 6.26-6.38 (3H, m), 7.02 (1H, dd, J=8.1, 7.9Hz), 8.07 (3H, brs), 9.38 (1H, s).

Table 1-55

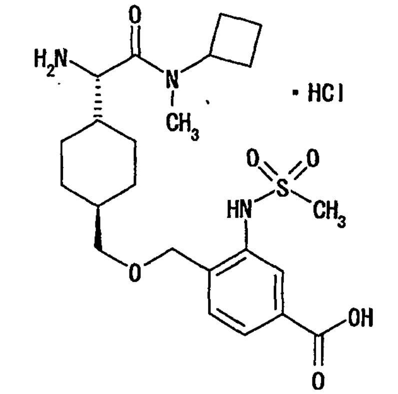
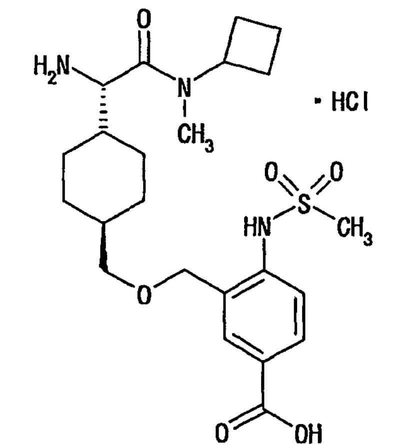
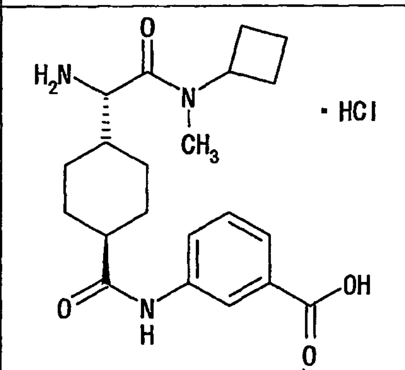
Example 203		^{1}H-NMR(δppm, DMSO-d_6) 0.80-1.30 (4H, m), 1.42-1.74 (6H, m), 1.74-1.87 (2H, m), 1.94-2.37 (4H, m), 2.89 (1.74H, s), 2.98 (1.26H, s), 3.01 (3H, s), 3.29 (2H, d, J=6.5Hz), 4.15 (0.42H, d, J=5.1Hz), 4.30 (0.58H, d, J=5.1Hz), 4.47-4.59 (0.58H, m), 4.63 (2H, s), 4.72-4.84 (0.42H, m), 7.54 (1H, d, J=8.1Hz), 7.82 (1H, d, J=8.1Hz), 7.88 (1H, s), 8.05 (3H, brs).
Example 204		^{1}H-NMR(δppm, DMSO-d_6) 0.82-1.31 (4H, m), 1.42-1.88 (8H, m), 1.94-2.37 (4H, m), 2.89 (1.74H, s), 2.98 (1.26H, s), 3.08 (3H, s), 3.28 (2H, d, J=6.0Hz), 4.15 (0.42H, d, J=5.0Hz), 4.30 (0.58H, d, J=5.0Hz), 4.47-4.59 (0.58H, m), 4.60 (2H, s), 4.72-4.84 (0.42H, m), 7.47 (1H, d, J=8.4Hz), 7.87 (1H, dd, J=8.4, 2.1Hz), 7.97 (1H, d, J=2.1Hz), 8.05 (3H, brs).
Example 205		^{1}H-NMR(δppm, DMSO-d_6) 1.06-1.50 (4H, m), 1.57-1.82 (5H, m), 1.85-2.37 (7H, m), 2.91 (1.74H, s), 3.01 (1.26H, s), 4.17-4.23 (0.42H, m), 4.32-4.38 (0.58H, m), 4.52-4.63 (0.58H, m), 4.73-4.84 (0.42H, m), 7.40 (1H, dd, J=7.9, 7.9Hz), 7.59 (1H, d, J=7.9Hz), 7.82 (1H, d, J=7.9Hz), 8.24 (1H, s), 10.12 (1H, brs).

Table 1-56

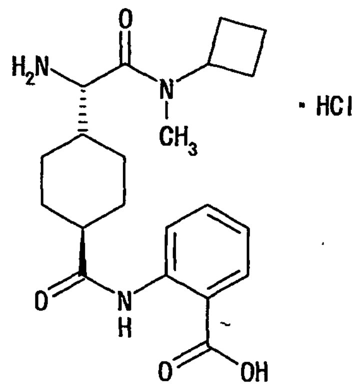
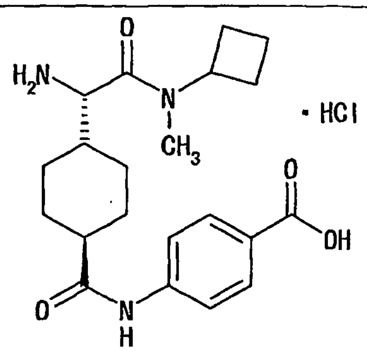
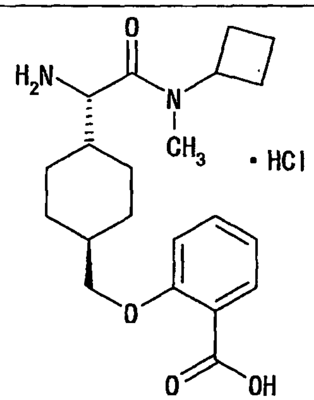
Example 206		^{1}H-NMR(δppm, DMSO-d_6) 1.14-1.49 (4H, m), 1.56-1.82 (5H, m), 1.94-2.36 (7H, m), 2.91 (1.74H, s), 3.01 (1.26H, s), 4.16-4.25 (0.42H, m), 4.31-4.38 (0.58H, m), 4.50-4.61 (0.58H, m), 4.73-4.84 (0.42H, m), 7.13 (1H, dd, J=8.4, 7.6Hz), 7.56 (1H, dd, J=8.0, 7.6Hz), 7.98 (1H, d, J=8.0Hz), 8.06 (3H, brs), 8.48 (1H, d, J=8.4Hz), 11.27 (1H, brs), 13.56 (1H, brs).
Example 207		^{1}H-NMR(δppm, DMSO-d_6) 1.06-1.50 (4H, m), 1.57-1.82 (5H, m), 1.85-2.40 (7H, m), 2.91 (1.74H, s), 3.01 (1.26H, s), 4.21 (0.42H, d, J=5.1Hz), 4.36 (0.58H, d, J=5.1Hz), 4.51-4.63 (0.58H, m), 4.73-4.84 (0.42H, m), 7.72 (2H, d, J=8.8Hz), 7.87 (2H, d, J=8.8Hz), 8.10 (3H, brs), 10.26 (1H, brs).
Example 208		^{1}H-NMR(δppm, DMSO-d_6) 0.95-1.32 (4H, m), 1.55-1.77 (6H, m), 1.84-2.37 (6H, m), 2.90 (1.74H, s), 2.99 (1.26H, s), 3.83 (2H, d, J=5.7Hz), 4.13-4.19 (0.42H, m), 4.28-4.34 (0.58H, m), 4.49-4.61 (0.58H, m), 4.72-4.85 (0.42H, m), 6.97 (1H, dd, J=7.4, 7.4Hz), 7.07 (1H, d, J=8.1Hz), 7.46 (1H, dd, J=8.1, 7.4Hz), 7.60 (1H, d, J=7.4Hz), 8.08 (3H, brs).

Table 1-57

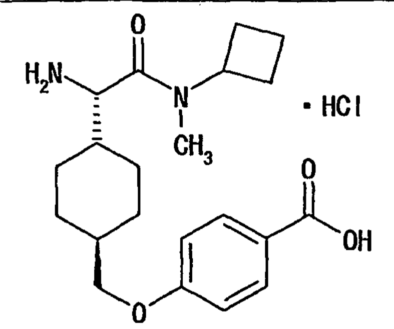
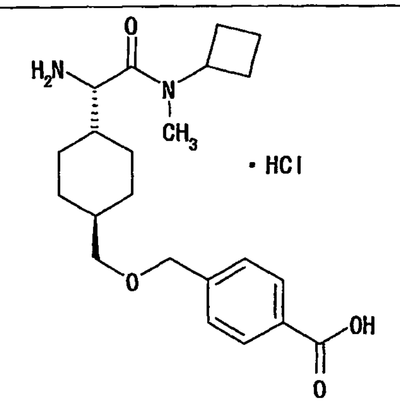
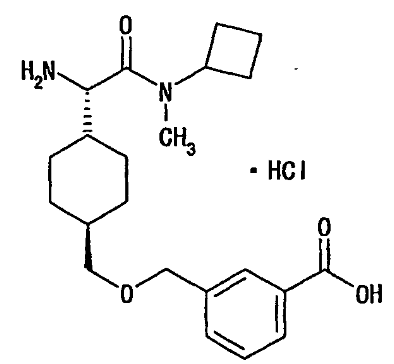
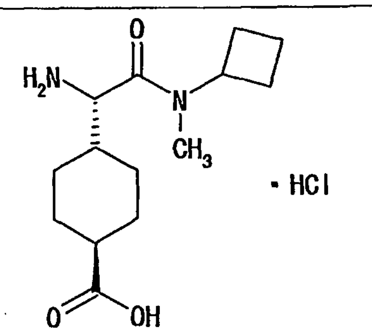
Example 209		^{1}H-NMR(δppm, DMSO-d_6) 0.90-1.34 (4H, m), 1.52-1.79 (6H, m), 1.80-2.38 (6H, m), 2.90 (1.74H, s), 2.99 (1.26H, s), 3.85 (2H, d, J=4.9Hz), 4.12-4.20 (0.42H, m), 4.27-4.36 (0.58H, m), 4.48-4.62 (0.58H, m), 4.72-4.85 (0.42H, m), 6.99 (2H, d, J=7.9Hz), 7.87 (2H, d, J=7.9Hz), 8.07 (3H, brs).
Example 210		^{1}H-NMR(δppm, DMSO-d_6) 0.81-1.29 (4H, m), 1.41-1.86 (8H, m), 1.94-2.36 (4H, m), 2.89 (1.74H, s), 2.98 (1.26H, s), 3.25 (2H, d, J=6.3Hz), 4.14 (0.42H, d, d=5.2Hz), 4.29 (0.58H, d, J=5.2Hz), 4.46-4.59 (0.58H, m), 4.52 (2H, s), 4.71-4.83 (0.42H, m), 7.42 (2H, d, J=8.4Hz), 7.92 (2H, d, J=8.4Hz), 8.06 (3H, brs).
Example 211		^{1}H-NMR(δppm, DMSO-d_6) 0.81-1.29 (4H, m), 1.41-1.86 (8H, m), 1.94-2.35 (4H, m), 2.89 (1.74H, s), 2.98 (1.26H, s), 3.25 (2H, d, J=6.5Hz), 4.14 (0.42H, d, d=5.1Hz), 4.29 (0.58H, d, J=5.1Hz), 4.44-4.60 (0.58H, m), 4.50 (2H, s), 4.71-4.83 (0.42H, m), 7.48 (1H, dd, J=7.4, 7.4Hz), 7.55 (1H, d, J=7.4Hz), 7.85 (1H, d, J=7.4Hz), 7.88 (1H, s), 8.07 (3H, brs).
Example 213		^{1}H-NMR(δppm, DMSO-d_6) 1.04-1.35 (4H, m), 1.52-1.78 (5H, m), 1.87-2.37 (7H, m), 2.89 (1.74H, s), 2.98 (1.26H, s), 4.15 (0.42H, d, J=5.2Hz), 4.30 (0.58H, d, J=5.2Hz), 4.48-4.59 (0.58H, m), 4.71-4.83 (0.42H, m), 8.14 (3H, brs).

Table 1-58

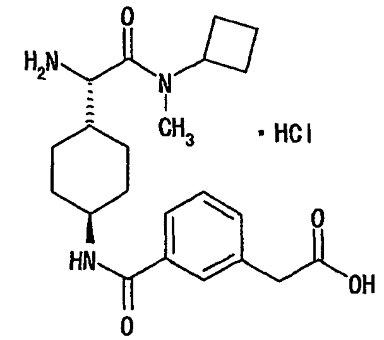
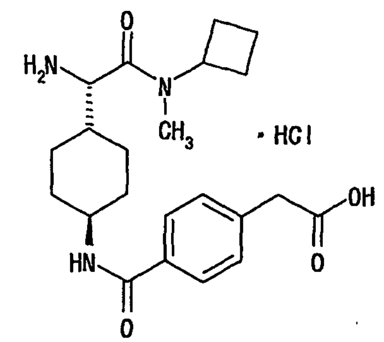
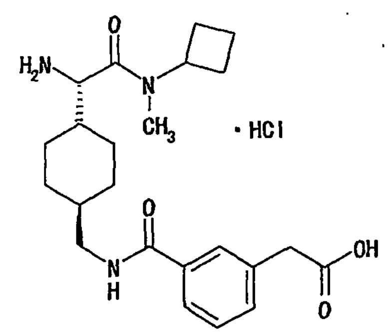
Example 214		^{1}H-NMR(δppm, DMSO-d_6) 1.15-1.39 (4H, m), 1.56-1.77 (5H, m), 1.82-1.94 (2H, m), 1.97-2.38 (4H, m), 2.91 (1.74H, s), 3.01 (1.26H, s), 3.62 (2H, s), 3.65-3.76 (1H, m), 4.18 (0.42H, d, J=5.7Hz), 4.34 (0.58H, d, J=5.7Hz), 4.51-4.63 (0.58H, m), 4.73-4.85 (0.42H, m), 7.35-7.42 (2H, m), 7.68-7.74 (2H, m), 8.10 (3H, brs), 8.22 (1H, d, J=7.9Hz).
Example 215		^{1}H-NMR(δppm, DMSO-d_6) 1.14-1.40 (4H, m), 1.57-1.77 (5H, m), 1.82-1.94 (2H, m), 1.97-2.38 (4H, m), 2.91 (1.74H, s), 3.01 (1.26H, s), 3.63 (2H, s), 3.65-3.75 (1H, m), 4.15-4.23 (0.42H, m), 4.30-4.38 (0.58H, m), 4.51-4.63 (0.58H, m), 4.73-4.84 (0.42H, m), 7.33 (2H, d, J=8.4Hz), 7.77 (2H, d, J=8.4Hz), 8.12 (3H, brs), 8.20 (1H, d, J=8.4Hz), 12.35 (1H, bs).
Example 216		^{1}H-NMR(δppm, DMSO-d_6) 0.79-1.26 (4H, m), 1.40-1.85 (8H, m), 1.93-2.36 (4H, m), 2.89 (1.74H, s), 2.98 (1.26H, s), 3.04-3.14 (2H, m), 3.63 (2H, s), 4.16 (0.42H, d, J=5.1Hz), 4.31 (0.58H, d, J=5.1Hz), 4.47-4.59 (0.58H, m), 4.71-4.83 (0.42H, m), 7.35-7.45 (2H, m), 7.68-7.76 (2H, m), 8.07 (3H, brs), 8.42-8.49 (1H, m).

Table 1-59

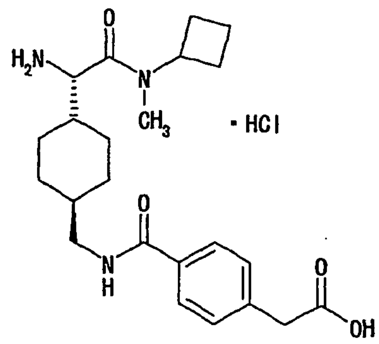
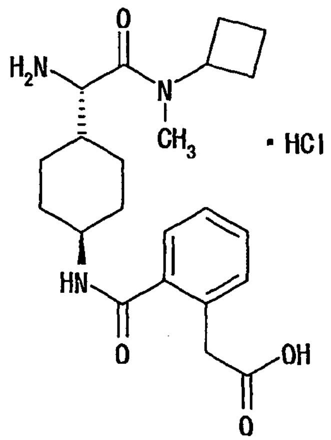
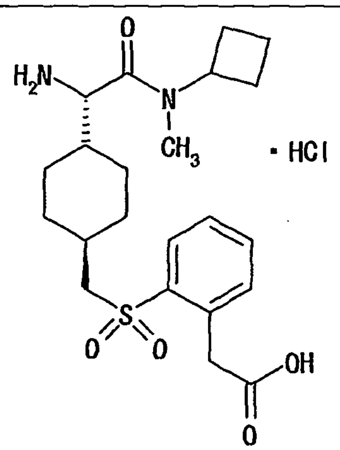
Example 217		^{1}H-NMR(δppm, DMSO-d_6) 0.78-1.30 (4H, m), 1.38-1.87 (8H, m), 1.93-2.36 (4H, m), 2.89 (1.74H, s), 2.98 (1.26H, s), 3.03-3.15 (2H, m), 3.63 (2H, s), 4.11-4.20 (0.42H, m), 4.26-4.36 (0.58H, m), 4.46-4.61 (0.58H, m), 4.69-4.83 (0.42H, m), 7.33 (2H, d, J=7.4Hz), 7.77 (2H, d, J=7.4Hz), 8.05 (3H, brs), 8.38-8.51 (1H, m).
Example 218		^{1}H-NMR(δppm, DMSO-d_6) 1.13-1.35 (4H, m), 1.55-1.74 (5H, m), 1.82-1.93 (2H, m), 1.96-2.36 (4H, m), 2.90 (1.74H, s), 3.00 (1.26H, s), 3.55-3.66 (1H, m), 3.75 (2H, s), 4.18 (0.42H, d, J=5.1Hz), 4.32 (0.58H, d, J=5.1Hz), 4.51-4.63 (0.58H, m), 4.72-4.83 (0.42H, m), 7.26-7.42 (4H, m), 8.08 (3H, bs), 8.20-8.26 (1H, m).
Example 219		^{1}H-NMR(δppm, DMSO-d_6) 0.91-1.31 (4H, m), 1.47-1.77 (5H, m), 1.80-2.36 (7H, m), 2.88 (1.74H, s), 2.96 (1.26H, s), 3.12-3.22 (2H, m), 4.06 (2H, s), 4.07-4.16 (0.42H, m), 4.22-4.31 (0.58H, m), 4.45-4.57 (0.58H, m), 4.69-4.82 (0.42H, m), 7.44-7.61 (2H, m), 7.64-7.75 (1H, m), 7.90 (1H, d, J=7.2Hz), 8.07 (3H, bs).

Table 1-60

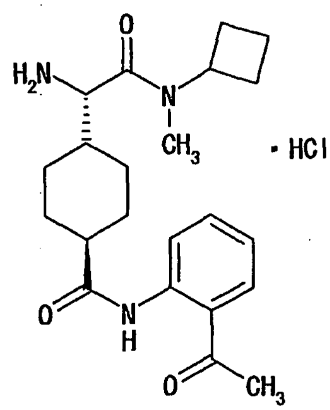
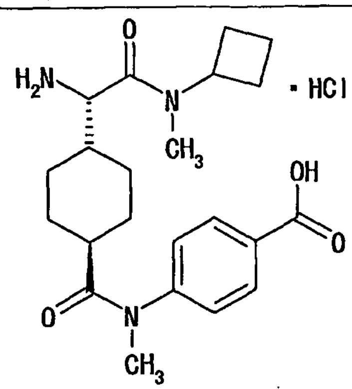
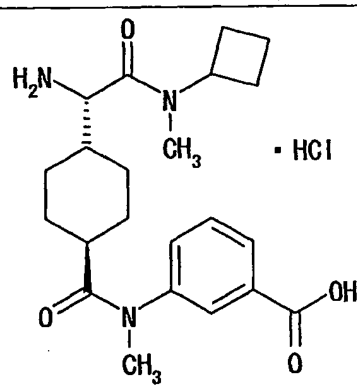
Example 220		^{1}H-NMR(δppm, DMSO-d_6) 1.13-1.49 (4H, m), 1.56-1.83 (5H, m), 1.93-2.37 (7H, m), 2.62 (3H, s), 2.91 (1.74H, s), 3.01 (1.26H, s), 4.16-4.23 (0.42H, m), 4.30-4.39 (0.58H, m), 4.51-4.62 (0.58H, m), 4.73-4.84 (0.42H, m), 7.20 (1H, dd, J=8.1, 7.4Hz), 7.59 (1H, dd, J=8.4, 7.4Hz), 800 (1H, d, J=8.1Hz), 8.13 (3H, bs), 8.36 (1H, d, J=8.4Hz), 11.35 (1H, s).
Example 221		^{1}H-NMR(δppm, DMSO-d_6) 0.76-1.05 (2H, m), 1.21-1.45 (2H, m), 1.45-1.80 (8H, m), 1.88-2.35 (4H, m), 2.86 (1.74H, s), 2.92 (1.26H, s), 3.16 (3H, s), 3.98-4.08 (0.42H, m), 4.14-4.24 (0.58H, m), 4.39-4.52 (0.58H, m), 4.67-4.80 (0.42H, m), 7.46 (2H, d, J=8.2Hz), 7.97 (3H, brs), 8.01 (2H, d, J=8.2Hz).
Example 222		^{1}H-NMR(δppm, DMSO-d_6) 0.71-1.04 (2H, m), 1.22-1.78 (8H, m), 1.89-2.37 (6H, m), 2.85 (1.74H, s), 2.92 (1.26H, s), 3.15 (3H, s), 3.97-4.09 (0.42H, m), 4.13-4.24 (0.58H, m), 4.38-4.52 (0.58H, m), 4.66-4.80 (0.42H, m), 7.53-7.67 (2H, m), 7.77-7.84 (1H, m), 7.87 (3H, brs), 7.94 (1H, s).

Table 1-61

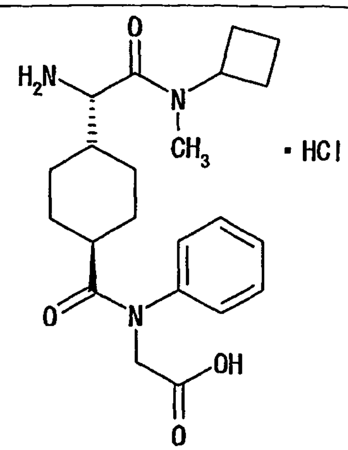
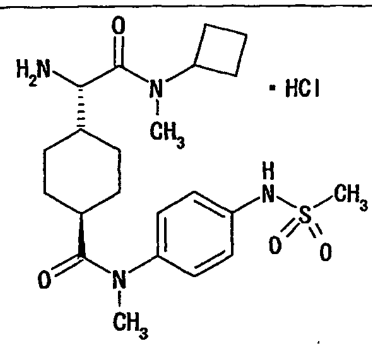
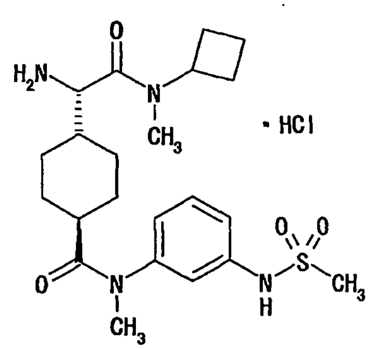
Example 223		^{1}H-NMR(δppm, DMSO-d_6) 0.72-1.03 (2H, m), 1.22-1.44 (2H, m), 1.44-1.79 (7H, m), 1.87-2.37 (5H, m), 2.85 (1.74H, s), 2.92 (1.26H, s), 3.99-4.07 (0.42H, m), 4.14-4.24 (0.58H, m), 4.20 (2H, s), 4.39-4.51 (0.58H, m), 4.66-4.79 (0.42H, m), 7.33-7.53 (5H, m), 8.06 (3H, bs).
Example 224		^{1}H-NMR(δppm, DMSO-d_6) 0.76-1.05 (2H, m), 1.21-1.42 (2H, m), 1.43-1.74 (8H, m), 1.93-2.32 (4H, m), 2.85 (1.74H, s), 2.92 (1.26H, s), 3.06 (3H, s), 3.08 (3H, s), 4.01-4.08 (0.42H, m), 4.15-4.22 (0.58H, m), 4.39-4.52 (0.58H, m), 4.67-4.80 (0.42H, m), 7.22-7.34 (4H, m), 7.94 (3H, bs).
Example 225		^{1}H-NMR(δppm, DMSO-d_6) 0.75-1.05 (2H, m), 1.23-1.45 (2H, m), 1.45-1.78 (8H, m), 1.88-2.35 (4H, m), 2.86 (1.74H, s), 2.93 (1.26H, s), 3.04 (3H, s), 3.11 (3H, s), 3.97-4.09 (0.42H, m), 4.15-4.24 (0.58H, m), 4.40-4.52 (0.58H, m), 4.67-4.81 (0.42H, m), 7.07 (1H, d, J=7.4Hz), 7.11 (1H, s), 7.20 (1H, d, J=7.7Hz), 7.43 (1H, dd, J=7.7, 7.4Hz), 7.94 (3H, brs).

Table 1-62

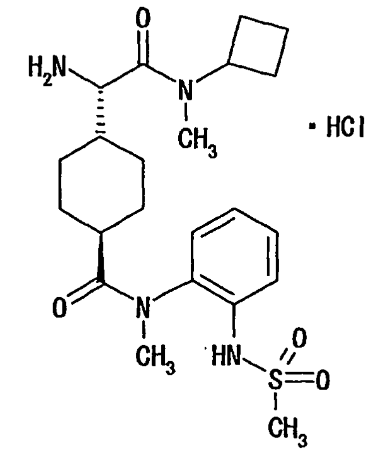
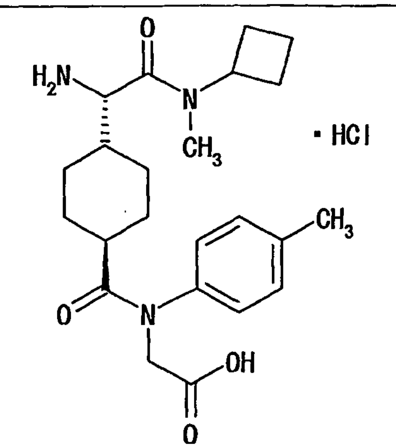
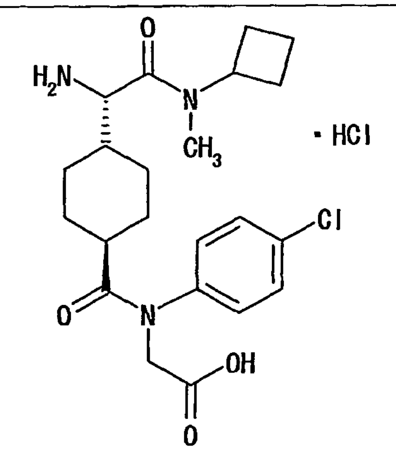
Example 226		^{1}H-NMR(δppm, DMSO-d_6) 0.66-1.04 (2H, m), 1.13-1.77 (8H, m), 1.77-2.36 (6H, m), 2.85 (1.74H, s), 2.92 (1.26H, s), 3.04 (3H, s), 3.15 (3H, s), 3.96-4.10 (0.42H, m), 4.11-4.24 (0.58H, m), 4.39-4.53 (0.58H, m), 4.66-4.82 (0.42H, m), 7.22 (1H, dd, J=7.5, 7.4Hz), 7.32 (1H, d, J=7.5Hz), 7.38 (1H, dd, J=8.1, 7.4Hz), 7.53 (1H, d, J=8.1Hz), 7.99 (3H, brs), 9.51 (1H, brs).
Example 227		^{1}H-NMR(δppm, DMSO-d_6) 0.75-1.04 (2H, m), 1.20-1.43 (2H, m), 1.43-1.77 (7H, m), 1.89-2.39 (5H, m), 2.33 (3H, s), 2.85 (1.74H, s), 2.92 (1.26H, s), 4.00-4.06 (0.42H, m), 4.14-4.22 (0.58H, m), 4.16 (2H, s), 4.40-4.52 (0.58H, m), 4.66-4.78 (0.42H, m), 7.21-7.33 (4H, m), 8.11 (3H, brs).
Example 228		^{1}H-NMR(δppm, DMSO-d_6) 0.78-1.06 (2H, m), 1.21-1.42 (2H, m), 1.44-1.76 (7H, m), 1.92-2.32 (5H, m), 2.85 (1.74H, s), 2.92 (1.26H, s), 4.01-4.05 (0.42H, m), 4.14-4.18 (0.58H, m), 4.20 (2H, s), 4.40-4.51 (0.58H, m), 4.67-4.78 (0.42H, m), 7.43 (2H, d, J=7.9Hz), 7.55 (2H, d, J=7.9Hz).

Table 1—63

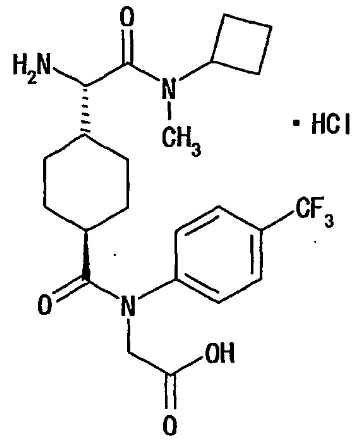
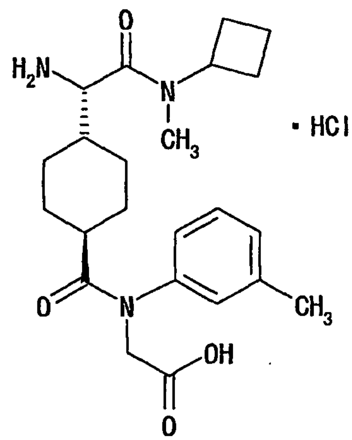
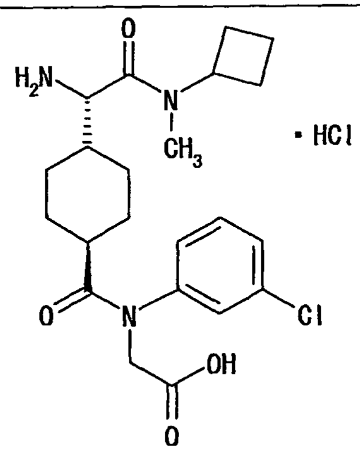
Example 229		^{1}H-NMR(δppm, DMSO-d_6) 0.73-1.07 (2H, m), 1.13-1.44 (2H, m), 1.45-1.83 (7H, m), 1.89-2.36 (5H, m), 2.85 (1.74H, s), 2.92 (1.26H, s), 3.99-4.08 (0.42H, m), 4.14-4.21 (0.58H, m), 4.26 (2H, s), 4.38-4.54 (0.58H, m), 4.66-4.79 (0.42H, m), 7.54-7.71 (2H, m), 7.78-7.93 (2H, m), 8.02 (3H, brs).
Example 230		^{1}H-NMR(δppm, DMSO-d_6) 0.75-1.05 (2H, m), 1.22-1.44 (2H, m), 1.45-1.78 (7H, m), 1.92-2.37 (5H, m), 2.33 (3H, s), 2.85 (1.74H, s), 2.92 (1.26H, s), 4.01-4.07 (0.42H, m), 4.14-4.21 (0.58H, m), 4.17 (2H, s), 4.40-4.52 (0.58H, m), 4.67-4.78 (0.42H, m), 7.12-7.25 (3H, m), 7.35 (1H, dd, J=8.1, 7.7Hz), 8.11 (3H, brs).
Example 231		^{1}H-NMR(δppm, DMSO-d_6) 0.77-1.06 (2H, m), 1.21-1.44 (2H, m), 1.46-1.79 (7H, m), 1.92-2.36 (5H, m), 2.86 (1.74H, s), 2.93 (1.26H, s), 4.02-4.07 (0.42H, m), 4.15-4.21 (0.58H, m), 4.22 (2H, s), 4.41-4.53 (0.58H, m), 4.67-4.79 (0.42H, m), 7.35-7.43 (1H, m), 7.45-7.57 (3H, m), 8.12 (3H, brs).

Table 1-64

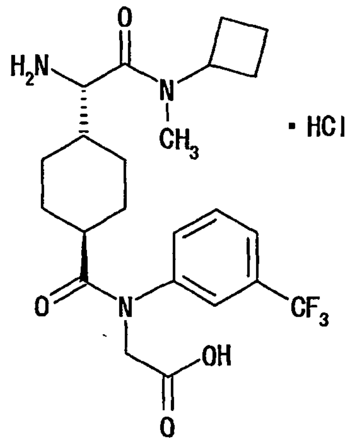
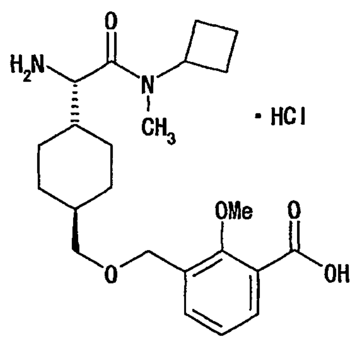
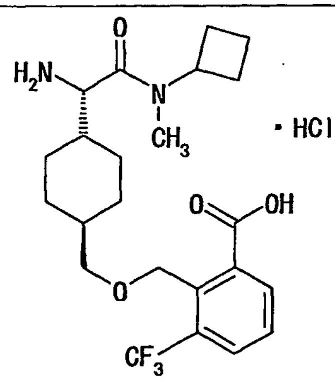
Example 232		^{1}H-NMR(δppm, DMSO-d_6) 0.72-1.04 (2H, m), 1.14-1.45 (2H, m), 1.46-1.81 (7H, m), 1.89-2.35 (5H, m), 2.85 (1.74H, s), 2.92 (1.26H, s), 4.00-4.08 (0.42H, m), 4.14-4.21 (0.58H, m), 4.27 (2H, s), 4.39-4.53 (0.58H, m), 4.65-4.79 (0.42H, m), 7.66-7.86 (4H, m), 8.02 (3H, brs).
Example 233		^{1}H-NMR(δppm, DMSO-d_6) 0.80-1.28 (4H, m), 1.41-1.88 (8H, m), 1.94-2.36 (4H, m), 2.88 (1.74H, s), 2.97 (1.26H, s), 3.28 (2H, d, J=6.0Hz), 3.75 (3H, s), 4.12 (0.42H, d, J=5.3Hz), 4.27 (0.58H, d, J=5.3Hz), 4.43-4.58 (0.58H, m), 4.48 (2H, s), 4.70-4.83 (0.42H, m), 7.19 (1H, dd, J=7.7, 7.4Hz), 7.53 (1H, d, J=7.4Hz), 7.63 (1H, d, J=7.7Hz).
Example 234		^{1}H-NMR(δppm, DMSO-d_6) 0.75-0.96(2H, m), 0.98-1.30(2H, m), 1.32-1.48(1H, m), 1.49-1.84(7H, m), 1.89-2.38(4H, m), 2.88(1.74H, s), 2.97(1.26H, s), 3.18(2H, d, J=6.0Hz), 4.09-4.17 (0.42H, m), 4.23-4.32(0.58H, m), 4.44-4.59(0.58H, m), 4.73(2H, s), 4.75-4.83(0.42H, m), 7.62(1H, t, J=7.5Hz), 7.83-7.90(2H, m), 8.04(3H, brs).

Table 1—65

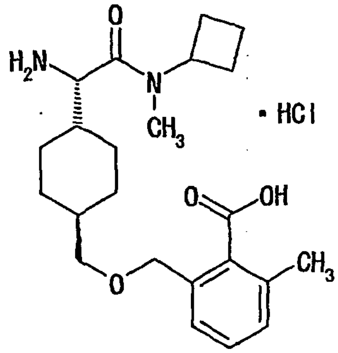
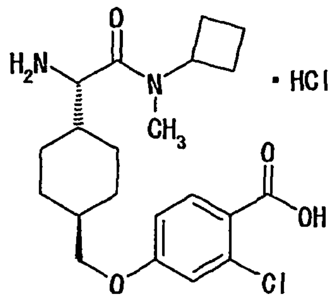
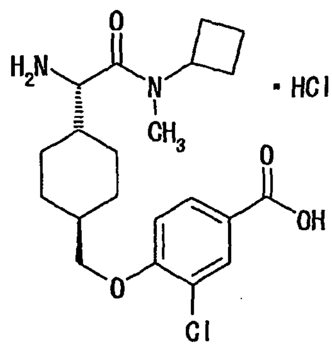
Example 235		^{1}H-NMR(δppm, DMSO-d_6) 0.77-0.99(2H, m), 1.02-1.33(2H, m), 1.35-1.51(1H, m), 1.52-1.85(7H, m), 1.92-2.36(4H, m), 2.29(3H, s), 2.89(1.70H, s), 2.98(1.30H, s), 3.18(2H, d, J=6.0Hz), 4.10-4.22(0.43H, m), 4.24-4.36(0.57H, m), 4.45(2H, s), 4.48-4.60(0.43H, m), 4.70-4.84(0.57H, m), 7.16-7.24(2H, m), 7.25-7.34(1H, m), 8.04(3H, brs), 13.03(1H, brs).
Example 236		^{1}H-NMR(δppm, DMSO-d_6) 0.91-1.34(4H, m), 1.55-1.78(6H, m), 1.81-1.93(2H, m), 1.95-2.37(4H, m), 2.90(1.65H, s), 2.99(1.35H, s), 3.87(2H, d, J=6.0Hz), 4.12-4.19(0.45H, m), 4.26-4.34(0.55H, m), 4.47-4.61(0.55H, m), 4.70-4.84 (0.45H, m), 6.97(1H, dd, J=3.0, 9.0Hz), 7.07(1H, d, J=3.0Hz), 7.83(1H, d, J=9.0Hz), 8.09(3H, brs).
Example 237		^{1}H-NMR(δppm, DMSO-d_6) 0.97-1.35(4H, m), 1.51-1.80(6H, m), 1.82-1.96(2H, m), 1.97-2.39(4H, m), 2.90(1.70H, s), 3.00(1.30H, s), 3.96(2H, d, J=6.0Hz), 4.13-4.19(0.43H, m), 4.27-4.34(0.57H, m), 4.48-4.63(0.57H, m), 4.72-4.85 (0.43H, m), 7.23(1H, d, J=9.0Hz), 7.88(1H, dd, J=9.0, 3.0Hz), 7.89(1H, s), 8.17(3H, brs).

Table 1—66

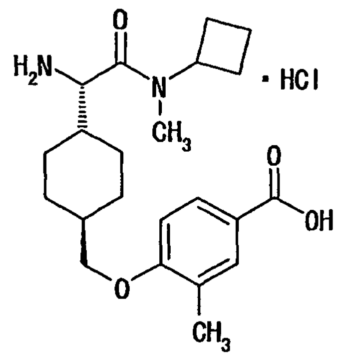
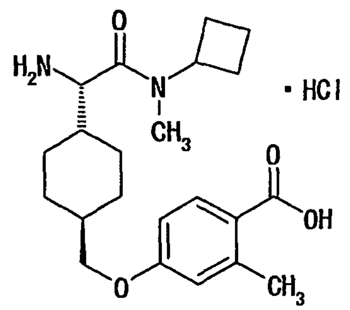
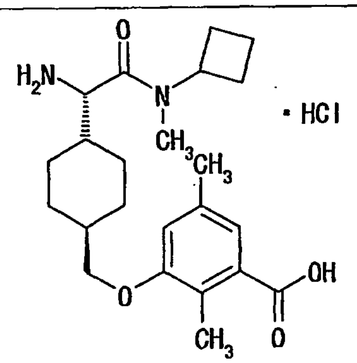
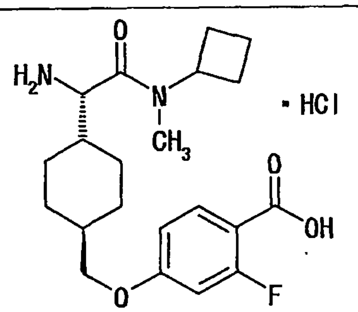
Example 239		^{1}H-NMR(δppm, DMSO-d_6) 0.95-1.35 (4H, m), 1.53-1.80 (6H, m), 1.83-1.95 (2H, m), 1.97-2.39 (4H, m), 2.18 (3H, s), 2.90 (1.73H, s), 3.00 (1.27H, s), 3.86 (2H, d, J=6.0Hz), 4.15 (0.42H, d, J=6.0Hz), 4.30 (0.58H, d, J=6.0Hz), 4.47-4.63 (0.58H, m), 4.68-4.85 (0.42H, m), 6.98 (1H, d, J=9.0Hz), 7.72 (1H, s), 7.76 (1H, dd, J=9.0, 3.0Hz), 8.13 (3H, brs).
Example 240		^{1}H-NMR(δppm, DMSO-d_6) 0.88-1.34 (4H, m), 1.53-1.79 (6H, m), 1.80-1.94 (2H, m), 1.96-2.38 (4H, m), 2.90 (1.69H, s), 2.99 (1.31H, s), 3.83 (2H, d, J=6.0Hz), 4.11-4.19 (0.44H, m), 4.24-4.34 (0.56H, m), 4.46-4.62 (0.56H, m), 4.69-4.85 (0.44H, m), 6.74-6.88 (2H, m), 7.82 (1H, d, J=9.0Hz).
Example 241		^{1}H-NMR(δppm, DMSO-d_6) 0.96-1.36(4H, m), 1.52-1.80(6H, m), 1.84-1.95(2H, m), 1.96-2.39(4H, m), 2.28(6H, s), 2.90(1.71H, s), 3.00(1.29H, s), 3.79 (2H, d, J=3.0Hz), 4.10-4.19 (0.43H, m), 4.26-4.34(0.57H, m), 4.47-4.62 (0.57H, m), 4.69-4.86(0.43H, m), 6.92 (1H, s), 7.11(1H, s), 8.25(3H, brs).
Example 243		^{1}H-NMR(δppm, DMSO-d_6) 0.89-1.34(4H, m), 1.52-1.78(6H, m), 1.80-1.93(2H, m), 1.94-2.40(4H, m), 2.90(1.70H, s), 2.99(1.30H, s), 3.87(2H, d, J=6.0Hz), 4.11-4.19(0.43H, m), 4.25-4.35(0.57H, m), 4.45-4.63 (0.57H, m), 4.67-4.86(0.43H, m), 6.77-6.93(2H, m), 7.81(1H, t, J=9.0Hz).

Table 1−67

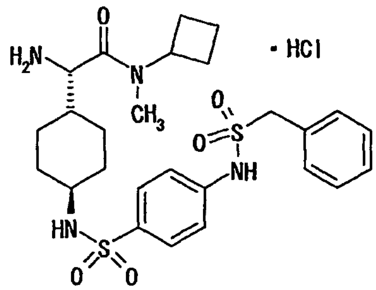
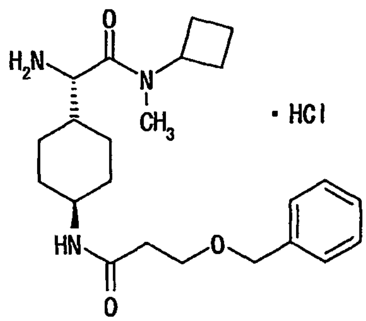
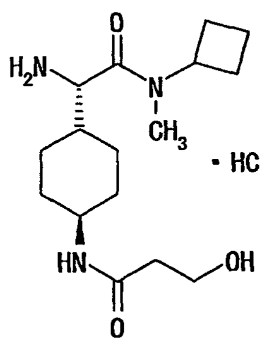
Example 244		^{1}H-NMR(δppm, DMSO-d_6) 10.39 (1H, s), 7.98 (3H, s), 7.70 (2H, d, J=8.7Hz), 7.58 (1H, t, J=7.7Hz), 7.34-7.33 (3H, m), 7.27-7.25 (4H, m), 4.72 (0.42H, t, J=9.2Hz), 4.60 (2H, s), 4.45 (0.58H, t, J=8.9Hz), 4.22 (0.58H, s), 4.05-4.03 (0.42H, m), 2.93 (1.27H, s), 2.85 (1.73H, s), 2.76-2.73 (1H, m), 2.21-2.06 (4H, m), 1.64-1.52 (7H, m), 1.17-1.09 (4H, m).
Example 245		^{1}H-NMR(δppm, DMSO-d_6) 8.08 (3.09H, s), 7.77 (1H, d, J=6.8Hz), 7.30 (5H, tt, J=12.4, 4.3Hz), 4.76 (0.45H, t, J=8.9Hz), 4.54 (0.55H, t, J=8.9Hz), 4.44 (2H, s), 4.32-4.28 (0.55H, m), 4.17-4.13 (0.45H, m), 3.62 (2H, t, J=6.2Hz), 3.44-3.41 (1H, m), 2.98 (1.34H, s), 2.89 (1.56H, s), 2.33-1.99 (6H, m), 1.78 (2H, s), 1.63 (5H, d, J=4.1Hz), 1.25-1.03 (4H, m).
Example 246		^{1}H-NMR(δppm, DMSO-d_6) 8.09 (3H, s), 7.68 (1H, d, J=4.6Hz), 4.75 (0.41H, t, J=7.9Hz), 4.53 (0.59H, t, J=8.8Hz), 4.29 (0.41H, brs), 4.14 (0.59H, brs), 3.59-3.57 (2H, m), 3.43 (1H, brs), 2.98 (1.24H, s), 2.89 (1.76H, s), 2.22-2.11 (6H, m), 1.79 (2H, brs), 1.63 (5H, brs), 1.35-1.05 (4H, m).

Table 1—68

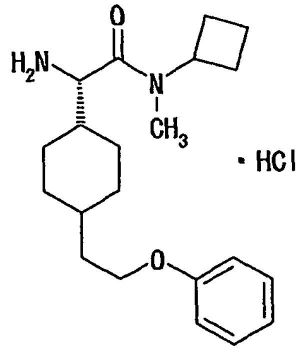
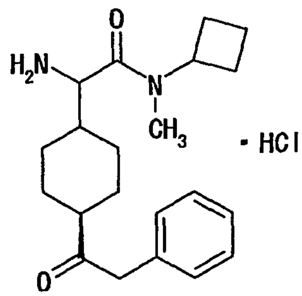
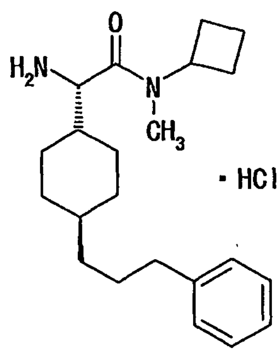
Example 247		^{1}H-NMR(δppm, DMSO-d_6) 7.96 (3H, brs), 7.25 (2H, t, J=7.9Hz), 6.90 (3H, dt, J=6.8, 2.6Hz), 4.76 (0.42H, t, J=9.2Hz), 4.57-4.49 (0.58H, m), 4.31-4.29 (0.52H, m), 4.16-4.11 (0.42H, m), 3.96 (2H, t, J=6.2Hz), 2.99 (1.25H, s), 2.88 (1.75H, s), 2.30-2.21 (1H, m), 2.10-1.99 (3H, m), 1.78-1.61 (9H, m), 1.36-1.33 (2H, m), 1.04 (3H, ddd, J=67.6, 25.1, 13.6Hz).
Example 248		^{1}H-NMR(δppm, DMSO-d_6) 8.04 (3H, brs), 7.33-7.14 (5H, m), 4.77 (0.43H, t, J=8.9Hz), 4.53 (0.57H, t, J=8.3Hz), 4.30 (0.57H, d, J=4.9Hz), 4.16 (0.43H, d, J=5.3Hz), 3.82 (2H, s), 2.97 (1.30H, s), 2.88 (1.70H, s), 2.26-2.04 (7H, m), 1.64-1.55 (5H, m), 1.20-1.16 (4H, m).
Example 249		^{1}H-NMR(δppm, DMSO-d_6) 8.01 (3H, brs), 7.26 (2H, t, J=7.3Hz), 7.17 (3H, d, J=7.2Hz), 4.77 (0.42H, t, J=9.0Hz), 4.52 (0.58H, t, J=8.7Hz), 4.28 (0.58H, d, J=5.3Hz), 4.13 (0.42H, d, J=4.9Hz), 2.97 (1.27H, s), 2.88 (1.73H, s), 2.56-2.47 (2H, m), 2.31-2.04 (4H, m), 1.73-1.61 (9H, m), 1.23-1.06 (5H, m), 0.84-0.80 (2H, m).

Table 1-69

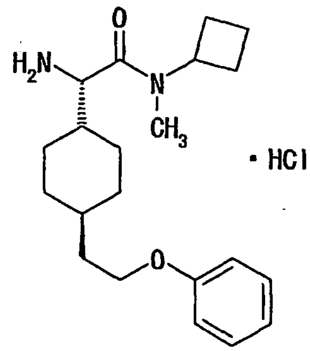
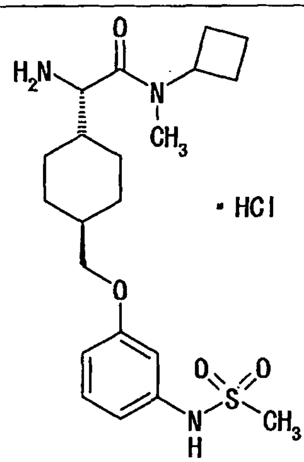
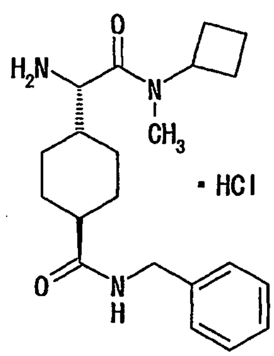
Example 250		^{1}H-NMR(δppm, DMSO-d_6) 8.06 (3H, brs), 7.27 (2H, t, J=7.9Hz), 6.92-6.90 (3H, m), 4.77 (0.42H, t, J=9.0Hz), 4.53 (0.58H, t, J=8.1Hz), 4.29 (0.58H, d, J=4.9Hz), 4.14 (0.42H, brs), 3.98 (2H, t, J=6.4Hz), 2.98 (1.25H, s), 2.89 (1.75H, s), 2.25-2.11 (4H, m), 1.81 (2H, d, J=11.3Hz), 1.60 (7H, dd, J=13.8, 7.3Hz), 1.40-1.36 (1H, m), 1.21-1.11 (2H, m), 0.93-0.89 (2H, m).
Example 251		^{1}H-NMR(δppm, DMSO-d_6) 9.72 (1H, s),8.07 (3H, brs), 7.21 (1H, t, J=8.5Hz), 6.77-6.76 (2H, m), 6.65 (1H, d, J=9.0Hz), 4.78 (0.45H, t, J=9.0Hz), 4.55 (0.55H, t, J=7.9Hz), 4.32 (0.55H, s), 4.18 (0.45H, s), 3.74 (2H, d, J=6.4Hz), 2.99 (1.36H, s), 2.97 (3H, s), 2.90 (1.64H, s), 2.29-2.06 (4H, m), 1.89-1.87 (2H, m), 1.65-1.55 (5H, m), 1.16-1.03 (4H, m).
Example 252		^{1}H-NMR(δppm, DMSO-d_6) 8.27 (1H, t, J=6.0Hz), 8.05 (3H, brs), 7.31-7.28 (2H, m), 7.23-7.19 (3H, m), 4.76 (0.40H, t, J=8.6Hz), 4.53 (0.60H, t, J=7.9Hz), 4.32 (0.60H, brs), 4.23 (2H, d, J=6.0Hz), 4.17 (0.40H, brs), 2.98 (1.21H, s), 2.89 (1.79H, s), 2.32-2.28 (1H, m), 2.17-2.08 (4H, m), 1.82-1.79 (2H, m), 1.63-1.61 (5H, m), 1.39-1.07 (4H, m).

Table 1—70

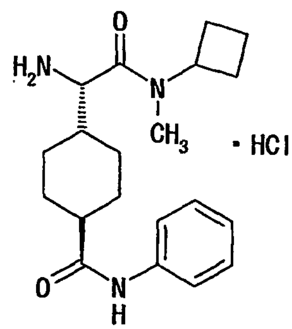
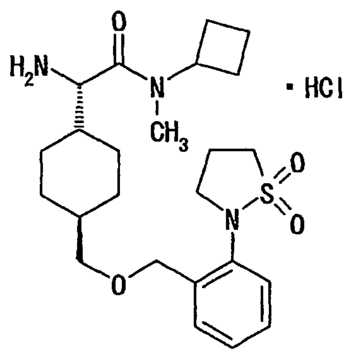
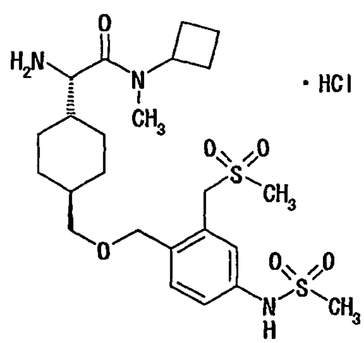
Example 253		^{1}H-NMR(δppm, DMSO-d_6) 9.87 (1H, s), 8.08 (3H, brs), 7.58 (2H, d, J=7.9Hz), 7.26 (2H, t, J=7.9Hz), 7.00 (1H, t, J=7.4Hz), 4.77 (0.44H, t, J=7.7Hz), 4.56 (0.56H, t, J=8.3Hz), 4.35 (0.56H, d, J=4.6Hz), 4.20 (0.44H, d, J=5.1Hz), 3.00 (1.32H, s), 2.90 (1.68H, s), 2.31-2.06 (5H, m), 1.90-1.86 (2H, m), 1.75-1.58 (5H, m), 1.36-1.14 (4H, m).
Example 254		^{1}H-NMR(δppm, DMSO-d_6) 8.00 (3H, brs), 7.50-7.37 (4H, m), 4.77 (0.42H, t, J=8.3Hz), 4.56-4.50 (0.58H, m), 4.56 (2H, s), 4.30 (0.58H, d, J=5.3Hz), 4.15 (0.42H, d, J=4.1Hz), 3.61 (2H, t, J=6.6Hz), 3.41 (2H, t, J=7.5Hz), 3.26 (2H, d, J=6.0Hz), 2.98 (1.25H, s), 2.89 (1.75H, s), 2.41 (2H, t, J=7.3Hz), 2.22-2.05 (4H, m), 1.82-1.79 (2H, m), 1.64-1.49 (6H, m), 1.28-1.07 (2H, m), 0.93-0.89 (2H, m).
Example 255		^{1}H-NMR(δppm, DMSO-d_6) 7.36 (1H, d, J=7.9Hz), 7.27 (1H, s), 7.17 (1H, d, J=8.3Hz), 4.79 (0.40H, t, J=8.7Hz), 4.56 (2H, s), 4.56-4.53 (0.60H, m), 4.53 (2H, s), 4.04-4.02 (0.60H, m), 3.92-3.88 (0.40H, m), 3.22 (2H, d, J=6.0Hz), 3.01 (3H, s), 3.00 (3H, s), 2.96 (1.21H, s), 2.87 (1.79H, s), 2.23-2.06 (4H, m), 1.76-1.46 (8H, m), 1.13-0.99 (4H, m).

Table 1—71

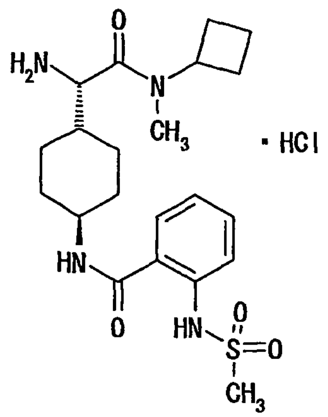
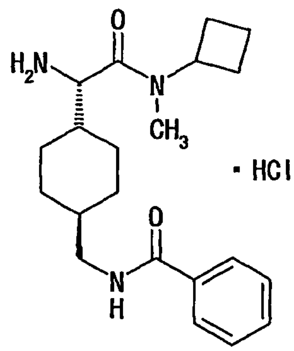
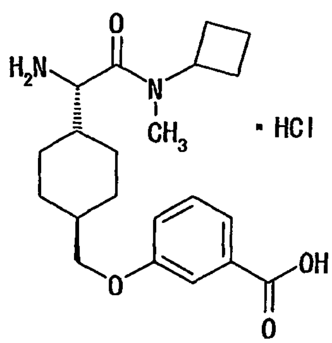
Example 256		^{1}H-NMR(δppm, DMSO-d_6) 11.06 (1H, d, J=10.5Hz), 8.62 (1H, d, J=7.9Hz), 8.10 (3H, brs), 7.81 (1H, d, J=8.3Hz), 7.52 (2H, t, J=5.8Hz), 7.19 (1H, brs), 4.79 (0.40H, t, J=8.9Hz), 4.57 (0.60H, t, J=7.9Hz), 4.35 (0.60H, brs), 4.20 (0.40H, brs), 3.71 (1H, brs), 3.11 (3H, s), 3.01 (1.20H, s), 2.91 (1.80H, s), 2.21-2.01 (6H, m), 1.68-1.65 (5H, m), 1.31-1.27 (4H, m).
Example 257		^{1}H-NMR(δppm, DMSO-d_6) 8.46 (1H, t, J=5.7Hz), 8.05 (3H, brs), 7.83 (2H, d, J=7.2Hz), 7.54-7.43 (3H, m), 4.77 (0.41H, t, J=8.1Hz), 4.53 (0.59H, t, J=7.3Hz), 4.31 (0.59H, brs), 4.16 (0.41H, brs), 3.09 (2H, t, J=6.0Hz), 2.98 (1.23H, s), 2.89 (1.76H, s), 2.23-2.14 (4H, m), 1.80-1.76 (2H, m), 1.60-1.51 (6H, m), 1.13-0.92 (4H, m).
Example 258		^{1}H-NMR(δppm, DMSO-d_6) 8.04 (3H, brs), 7.51 (1H, d, J=7.5Hz), 7.40-7.39 (2H, m), 7.17 (1H, dd, J=8.5, 1.7Hz), 4.78 (0.42H, t, J=9.0Hz), 4.55 (0.58H, t, J=7.9Hz), 4.32 (0.58H, d, J=4.5Hz), 4.17 (0.42H, d, J=4.9Hz), 3.83 (2H, d, J=6.0Hz), 2.99 (1.27H, s), 2.90 (1.73H, s), 2.22-2.10 (3H, m), 1.91-1.88 (2H, m), 1.68-1.65 (6H, m), 1.22-1.09 (5H, m).

Table 1—72

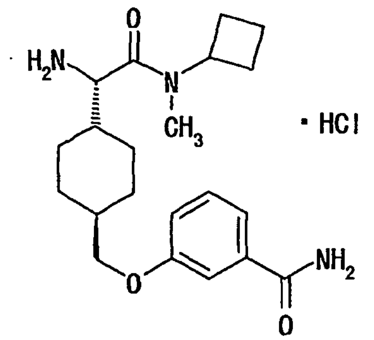
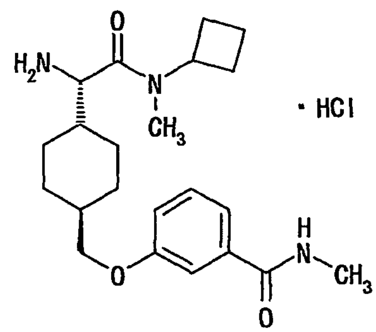
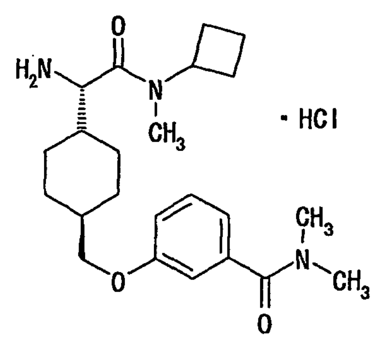
Example 259		^{1}H-NMR(δppm, DMSO-d_6) 8.03 (3H, brs), 7.95 (1H, brs), 7.42-7.33 (4H, m), 7.06-7.05 (1H, m), 4.81-4.77 (0.42H, m), 4.58-4.51 (0.58H, m), 4.36-4.34 (0.58H, m), 4.19-4.15 (0.42H, m), 3.83 (2H, t, J=7.5Hz), 2.99 (1.26H, s), 2.90 (1.74H, s), 2.32-2.27 (1H, m), 2.22-1.96 (2H, m), 1.94-1.87 (2H, m), 1.76-1.56 (6H, m), 1.28-0.97 (5H, m).
Example 260		^{1}H-NMR(δppm, DMSO-d_6) 8.40 (1H, d, J=4.5Hz), 8.04 (3H, brs), 7.41-7.31 (3H, m), 7.06-7.03 (1H, m), 4.80-4.78 (0.40H, m), 4.55-4.52 (0.60H, m), 4.32 (0.60H, s), 4.19 (0.40H, s), 3.82 (2H, d, J=6.4Hz), 3.00 (1.20H, s), 2.90 (1.80H, s), 2.77 (3H, d, J=4.5Hz), 2.27-2.05 (3H, m), 1.91 (2H, s), 1.65 (6H, s), 1.28-0.99 (5H, m).
Example 261		^{1}H-NMR(δppm, DMSO-d_6) 8.04 (3H, brs), 7.32 (1H, t, J=7.9Hz), 6.98-6.89 (3H, m), 4.78 (0.40H, t, J=7.9Hz), 4.54 (0.60H, t, J=7.7Hz), 4.31 (0.60H, d, J=6.0Hz), 4.17 (0.40H, d, J=4.9Hz), 3.80 (2H, d, J=6.0Hz), 2.99 (1.20H, s), 2.96 (3H, brs), 2.90 (1.80H, s), 2.88 (3H, brs), 2.22-2.04 (4H, m), 1.91-1.87 (2H, m), 1.66-1.61 (6H, m), 1.27-0.98 (4H, m).

Table 1-73

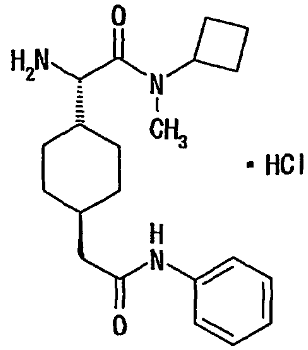
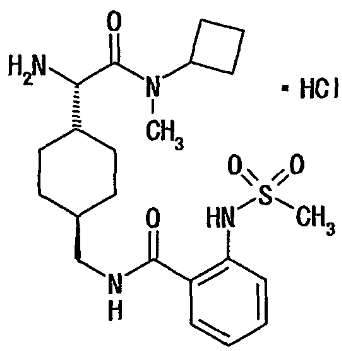
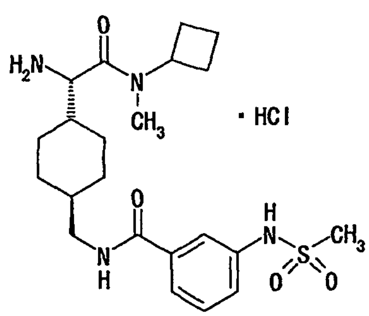
Example 262		^{1}H-NMR(δppm, DMSO-d_6) 9.88 (1H, s), 8.03 (3H, brs), 7.58 (2H, d, J=7.5Hz), 7.27 (3H, t, J=7.9Hz), 7.02 (1H, t, J=7.3Hz), 4.77 (0.42H, t, J=9.2Hz), 4.53 (0.58H, t, J=8.5Hz), 4.31 (0.58H, brs), 4.16 (0.42H, brs), 2.98 (1.27H, s), 2.89 (1.73H, s), 2.27-2.11 (5H, m), 1.77-1.64 (8H, m), 1.24-0.86 (4H, m).
Example 263		^{1}H-NMR(δppm, DMSO-d_6) 11.18 (1H, s), 8.89 (1H, s), 8.04 (3H, s), 7.83 (1H, d, J=8.3Hz), 7.54-7.53 (2H, m), 7.21-7.16 (1H, m), 4.77 (0.42H, t, J=9.0Hz), 4.53 (0.58H, t, J=7.7Hz), 4.30 (0.58H, brs), 4.17 (0.42H, brs), 3.13-3.10 (2H, m), 3.11 (3H, s), 2.98 (1.25H, s), 2.89 (1.75H, s), 2.23-2.09 (4H, m), 1.81-1.50 (8H, m), 1.11-0.96 (4H, m).
Example 264		^{1}H-NMR(δppm, DMSO-d_6) 9.88 (1H, s), 8.48 (1H, t, J=5.3Hz), 8.04 (3H, brs), 7.65 (1H, s), 7.55 (1H, d, J=7.2Hz), 7.41 (1H, t, J=7.7Hz), 7.34 (1H, d, J=9.0Hz), 4.77 (0.44H, t, J=7.9Hz), 4.53 (0.56H, t, J=7.9Hz), 4.30 (0.56H, brs), 4.16 (0.44H, brs), 3.08 (2H, t, J=6.2Hz), 3.01 (3H, s), 2.98 (1.31H, s), 2.89 (1.69H, s), 2.32-2.00 (4H, m), 1.78-1.63 (7H, m), 1.46 (1H, s), 1.15-0.89 (4H, m).

Table 1-74

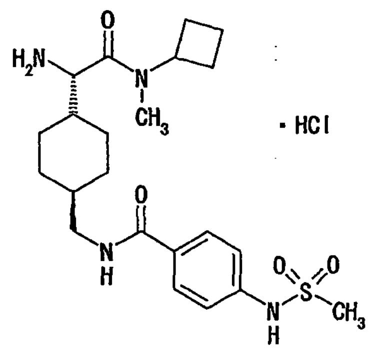
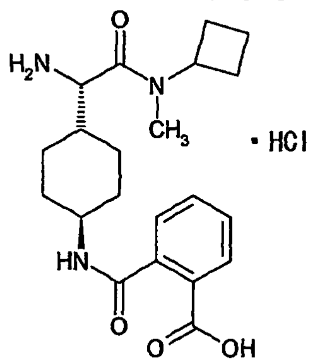
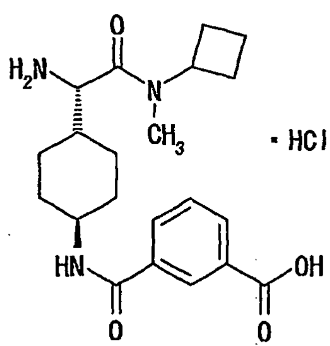
Example 265		^{1}H-NMR(δppm, DMSO-d_6) 10.09 (1H, s), 8.37 (1H, brs), 8.03 (3H, brs), 7.81 (2H, d, J=8.7Hz), 7.23 (2H, d, J=8.7Hz), 4.77 (0.41H, t, J=9.6Hz), 4.53 (0.59H, brs), 4.31 (0.59H, brs), 4.16 (0.41H, brs), 3.07-3.05 (2H, m), 3.05 (3H, s), 2.98 (1.22H, s), 2.89 (1.78H, s), 2.32-2.00 (4H, m), 1.78-1.63 (7H, m), 1.46-1.43 (1H, m), 1.18-1.08 (3H, m), 0.92-0.88 (1H, m).
Example 266		^{1}H-NMR(δppm, DMSO-d_6) 8.14-8.05 (4H, m), 7.76 (1H, d, J=7.5Hz), 7.54-7.50 (2H, m), 7.35 (1H, dd, J=7.5, 1.1Hz), 4.80-4.76 (0.43H, m), 4.57-4.54 (0.57H, m), 4.33 (0.57H, brs), 4:20 (0.43H, brs), 3.61-3.57 (1H, m), 3.00 (1.29H, s), 2.91 (1.71H, s), 2.35-1.91 (6H, m), 1.66-1.65 (5H, m), 1.29-1.07 (4H, m).
Example 267		^{1}H-NMR(δppm, DMSO-d_6) 8.46 (1H, d, J=7.9Hz), 8.39 (1H, d, J=1.9Hz), 8.05 (1H, dd, J=7.7, 1.6Hz), 8.05 (3H, brs), 7.58 (1H, t, J=7.7Hz), 4.78 (0.40H, t, J=9.7Hz), 4.56 (0.60H, t, J=7.9Hz), 4.33 (0.60H, d, J=5.6Hz), 4.18 (0.40H, d, J=6.0Hz), 3.71 (1H, brs), 3.00 (1.19H, s), 2.90 (1.81H, s), 2.30-2.28 (1H, m), 2.21-2.06 (3H, m), 1.90-1.88 (2H, m), 1.65-1.64 (5H, m), 1.30-1.27 (4H, m).

Table 1-75

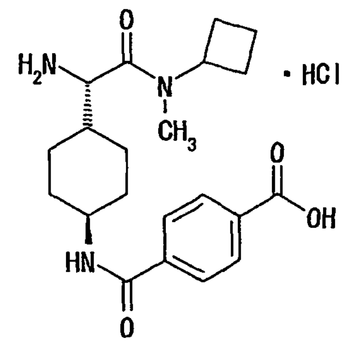
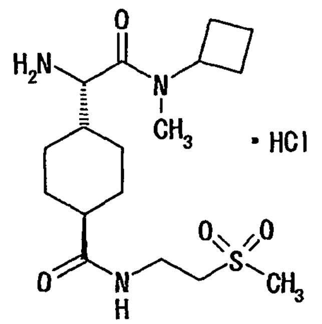
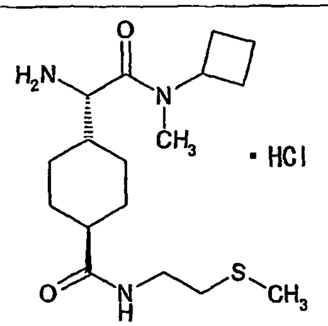
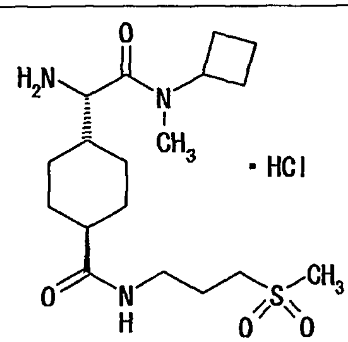
Example 268		^{1}H-NMR(δppm, DMSO-d_6) 8.41 (1H, d, J=8.3Hz), 7.99 (2H, d, J=8.3Hz), 7.95 (3H, brs), 7.91 (2H, d, J=8.3Hz), 4.79-4.77 (0.38H, m), 4.57-4.55 (0.62H, m), 4.33 (0.62H, d, J=5.6Hz), 4.18 (0.38H, d, J=5.6Hz), 3.71 (1H, brs), 3.00 (1.14H, s), 2.90 (1.86H, s), 2.30-2.28 (1H, m), 2.15-2.04 (3H, m), 1.90-1.88 (2H, m), 1.65-1.64 (5H, m), 1.26-1.19 (4H, m).
Example 269		^{1}H-NMR(δppm, DMSO-d_6) 8.04 (4H, s), 4.79-4.75 (0.47H, m), 4.55-4.52 (0.53H, m), 4.31 (0.53H, brs), 4.18 (0.47H, brs), 3.43 (2H, q, J=6.4Hz), 3.21 (2H, t, J=6.4Hz), 2.26-1.99 (4H, m), 1.71-1.65 (8H, m), 1.26-1.14 (4H, m).
Example 270		^{1}H-NMR(δppm, DMSO-d_6) 8.04 (3H, brs), 7.88 (1H, t, J=5.1Hz), 4.77-4.74 (0.57H, m), 4.55-4.52 (0.43H, m), 4.33 (0.57H, brs), 4.19 (0.43H, brs), 3.20 (2H, q, J=6.7Hz), 2.98 (1.30H, s), 2.89 (1.70H, s), 2.49 (2H, t, J=6.7Hz), 2.27-1.99 (5H, m), 2.05 (3H, s), 1.76-1.64 (7H, m), 1.32-1.09 (4H, m).
Example 271		^{1}H-NMR(δppm, DMSO-d_6) 8.03 (3H, brs), 7.85 (1H, t, J=6.4Hz), 4.79-4.76 (0.48H, m), 4.55-4.52 (0.52H, m), 4.32 (0.52H, brs), 4.18 (0.48H, brs), 3.13-3.06 (4H, m), 2.99 (1.43H, s), 2.95 (3H, s), 2.90 (1.57H, s), 2.23-2.03 (5H, m), 1.77-1.63 (9H, m), 1.29-1.09 (4H, m).

Table 1-76

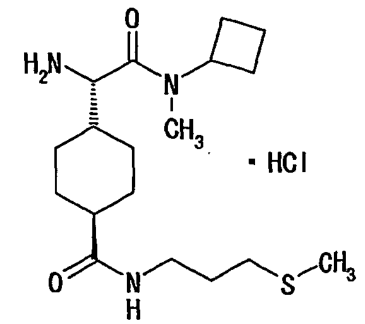
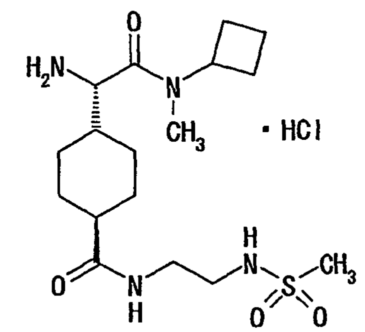
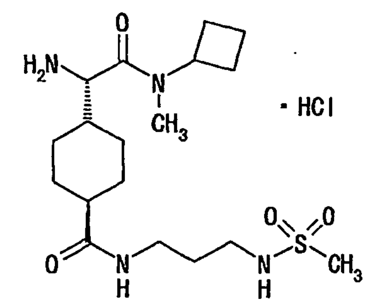
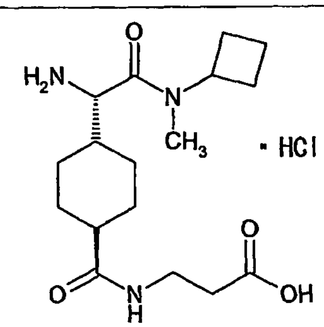
Example 272		^{1}H-NMR(δppm, DMSO-d_6) 8.04 (3H, brs), 7.76 (1H, t, J=5.8Hz), 4.77 (0.41H, t, J=8.1Hz), 4.54 (0.59H, t, J=7.9Hz), 4.33 (0.59H, brs), 4.18 (0.41H, brs), 3.08 (2H, q, J=6.5Hz), 2.98 (1.24H, s), 2.89 (1.76H, s), 2.43 (2H, t, J=7.3Hz), 2.32-1.95 (5H, m), 2.02 (3H, s), 1.76-1.60 (9H, m), 1.23 (4H, tt, J=30.3, 11.9Hz).
Example 273		^{1}H-NMR(δppm, DMSO-d_6) 8.05 (3H, brs), 7.85 (1H, t, J=5.7Hz), 7.05 (1H, t, J=6.2Hz), 4.79-4.76 (0.37H, m), 4.54-4.52 (0.63H, m), 4.32 (0.63H, brs), 4.17 (0.37H, brs), 3.11 (2H, q, J=6.4Hz), 2.98 (1.11H, s), 2.96 (2H, t, J=7.3Hz), 2.89 (1.89H, s), 2.88 (3H, s), 2.30-2.00 (5H, m), 1.77-1.64 (7H, m), 1.32-1.07 (4H, m).
Example 274		^{1}H-NMR(δppm, DMSO-d_6) 8.05 (3H, brs), 7.76 (1H, brs), 6.94 (1H, t, J=5.3Hz), 4.78-4.76 (0.44H, m), 4.56-4.53 (0.56H, m), 4.32 (0.56H, brs), 4.18 (0.44H, brs), 3.05 (2H, q, J=6.3Hz), 2.98 (1.32H, s), 2.90 (2H, q, J=7.3Hz), 2.89 (1.68H, s), 2.87 (3H, s), 2.23-2.06 (5H, m), 1.71-1.57 (9H, m), 1.24-1.13 (4H, m).
Example 275		^{1}H-NMR(δppm, DMSO-d_6) 12.16 (1H, brs), 8.04 (3H, brs), 7.82 (1H, t, J=5.5Hz), 4.78-4.75 (0.41H, m), 4.54-4.51 (0.59H, m), 4.32 (0.59H, brs), 4.17 (0.41H, brs), 3.20 (2H, q, J=6.3Hz), 2.98 (1.23H, s), 2.89 (1.77H, s), 2.34 (2H, t, J=6.8Hz), 2.26-2.10 (4H, m), 1.75-1.60 (8H, m), 1.23-1.14 (4H, m).

Table 1-77

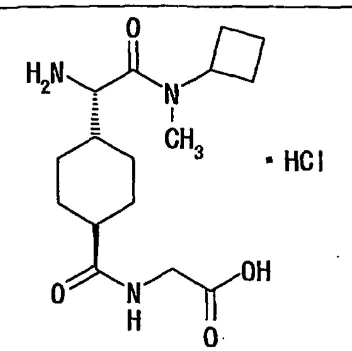
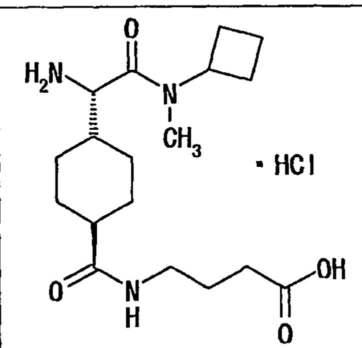
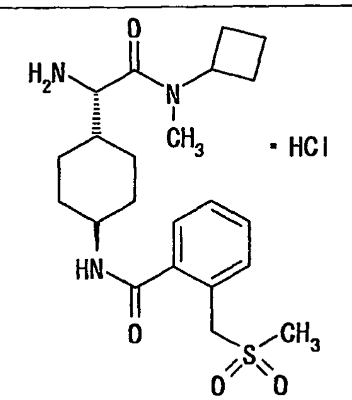
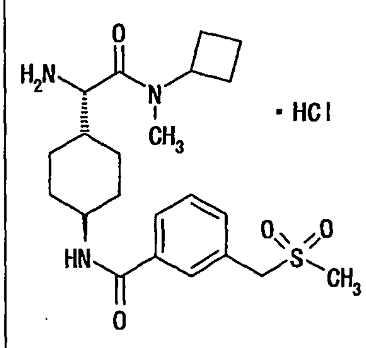
Example 276		^{1}H-NMR(δppm, DMSO-d_6) 8.09 (2.46H, t, J=6.0Hz), 8.05 (3H, brs), 4.77 (0.41H, t, J=9.2Hz), 4.54 (0.59H, t, J=8.5Hz), 4.32 (0.59H, d, J=3.8Hz), 4.17 (0.41H, d, J=5.3Hz), 3.70 (2H, d, J=5.7Hz), 2.99 (1.23H, s), 2.90 (1.77H, s), 2.21-2.05 (5H, m), 1.73-1.66 (7H, m), 1.24-1.15 (4H, m).
Example 277		^{1}H-NMR(δppm, DMSO-d_6) 12.04 (1H, brs), 8.04 (3H, brs), 7.74 (1H, t, J=5.7Hz), 4.77 (0.43H, t, J=8.5Hz), 4.54 (0.57H, t, J=7.9Hz), 4.33 (0.57H, brs), 4.18 (0.43H, brs), 3.01 (2H, q, J=6.2Hz), 2.98 (1.29H, s), 2.89 (1.71H, s), 2.27-1.91 (5H, m), 2.19-2.16 (2H, m), 1.72-1.60 (9H, m), 1.24-1.15 (4H, m).
Example 278		^{1}H-NMR(δppm, DMSO-d_6) 8.34-8.32 (1H, m), 8.07 (3H, brs), 7.50-7.42 (4H, m), 4.79 (2H, s), 4.77-4.73 (0.43H, m), 4.57-4.54 (0.57H, m), 4.33 (0.57H, brs), 4.20 (0.43H, brs), 3.63 (1H, brs), 3.00 (1.30H, s), 2.91 (1.70H, s), 2.86 (3H, s), 2.16-2.03 (6H, m), 1.67-1.66 (5H, m), 1.30-1.26 (4H, m).
Example 279		^{1}H-NMR(δppm, DMSO-d_6) 8.30 (1H, d, J=7.9Hz), 8.10 (3H, brs), 7.86-7.83 (2H, m), 7.55 (1H, d, J=7.5Hz), 7.48 (1H, t, J=7.3Hz), 4.77 (0.36H, d, J=8.7Hz), 4.60-4.54 (0.64H, m), 4.54 (2H, s), 4.34 (0.64H, brs), 4.19 (0.36H, brs), 3.73 (1H, brs), 3.01 (1.07H, s), 2.93 (3H, s), 2.91 (1.93H, s), 2.30-2.00 (4H, m), 1.91-1.89 (2H, m), 1.68-1.64 (5H, m), 1.30-1.26 (4H, m).

Table 1-78

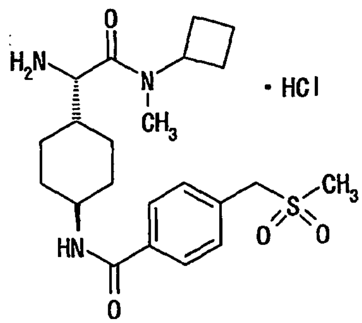
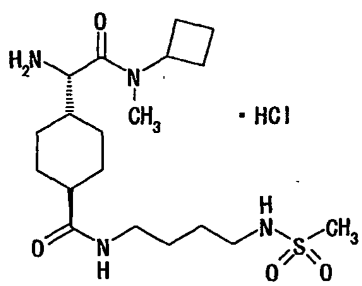
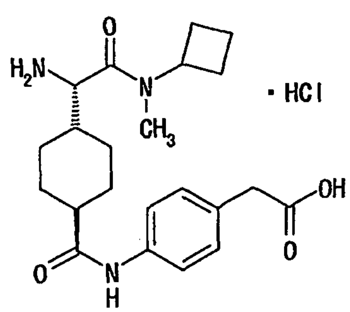
Example 280		[1]H-NMR(δppm, DMSO-d$_6$) 8.27 (1H, d, J=7.9Hz), 8.08 (3H, brs), 7.84 (2H, d, J=7.9Hz), 7.48 (2H, d, J=8.3Hz), 4.79 (0.35H, t, J=9.0Hz), 4.57-4.53 (0.65H, m), 4.55 (2H, s), 4.35 (0.65H, brs), 4.20 (0.35H, brs), 3.71 (1H, brs), 3.01 (1.05H, s), 2.91 (4.95H, s), 2.23-2.07 (4H, m), 1.91-1.88 (2H, m), 1.68-1.65 (5H, m), 1.30-1.27 (4H, m).
Example 281		[1]H-NMR(δppm, DMSO-d$_6$) 8.05 (3H, brs), 7.73 (1H, t, J=5.8Hz), 6.94 (1H, t, J=5.7Hz), 4.77-4.74 (0.44H, m), 4.57-4.54 (0.56H, m), 4.31 (0.56H, brs), 4.18 (0.44H, brs), 3.01-2.98 (2H, m), 2.98 (1.32H, s), 2.89-2.86 (2H, m), 2.89 (1.68H, s), 2.86 (3H, s), 2.21-2.03 (5H, m), 1.69-1.64 (7H, m), 1.30-1.18 (8H, m).
Example 282		[1]H-NMR(δppm, DMSO-d$_6$) 9.81 (1H, s), 8.03 (3H, brs), 7.51 (2H, d, J=8.7Hz), 7.15 (2H, d, J=8.7Hz), 4.79-4.77 (0.45H, m), 4.58-4.55 (0.55H, m), 4.37-4.37 (0.55H, m), 4.24-4.21 (0.44H, m), 3.49 (2H, s), 3.00 (1.35H, s), 2.91 (1.65H, s), 2.28-1.99 (5H, m), 1.91-1.86 (2H, m), 1.68-1.65 (5H, m), 1.41-1.07 (4H, m).

Table 1-79

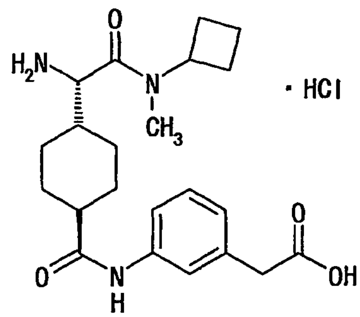
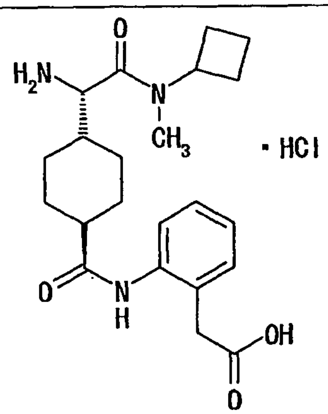
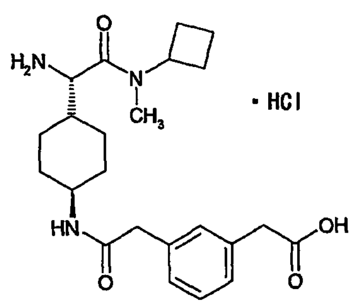
Example 283		^{1}H-NMR(δppm, DMSO-d_6) 9.84 (1H, s), 8.15 (3H, brs), 7.51 (1H, s), 7.48 (1H, d, J=7.9Hz), 7.21 (1H, t, J=7.7Hz), 6.91 (1H, d, J=7.2Hz), 4.80-4.77 (0.43H, m), 4.58-4.55 (0.57H, m), 4.35 (0.57H, d, J=4.9Hz), 4.21 (0.43H, d, J=5.3Hz), 3.50 (2H, s), 3.00 (1.28H, s), 2.91 (1.72H, s), 2.20-2.10 (5H, m), 1.91-1.86 (2H, m), 1.68-1.64 (5H, m), 1.42-1.07 (4H, m).
Example 284		^{1}H-NMR(δppm, DMSO-d_6) 9.32 (1H, s), 8.03 (3H, brs), 7.33 (1H, d, J=7.9Hz), 7.24-7.21 (2H, m), 7.13 (1H, t, J=7.3Hz), 4.79-4.78 (0.39H, m), 4.57-4.54 (0.61H, m), 4.36 (0.61H, brs), 4.21 (0.39H, brs), 3.57 (2H, s), 3.01 (1.18H, s), 2.91 (1.82H, s), 2.27-1.99 (5H, m), 1.90-1.87 (2H, m), 1.68-1.64 (5H, m), 1.30-1.14 (4H, m).
Example 285		^{1}H-NMR(δppm, DMSO-d_6) 8.03-7.97 (4H, m), 7.22-7.20 (1H, m), 7.13-7.10 (3H, m), 4.78-4.76 (0.39H, m), 4.55-4.51 (0.61H, m), 4.31 (0.61H, brs), 4.16 (0.39H, brs), 3.54-3.52 (1H, m), 3.52 (2H, s), 3.33 (2H, s), 2.98 (1.16H, s), 2.89 (1.84H, s), 2.28-1.99 (4H, m), 1.85-1.82 (2H, m), 1.63-1.60 (5H, m), 1.17-1.09 (4H, m).

Table 1-80

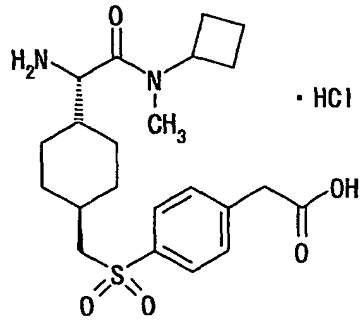
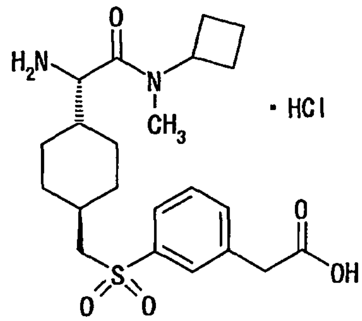
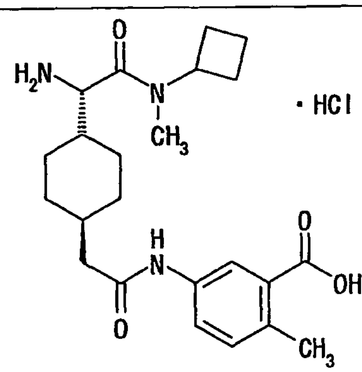
Example 286		^{1}H-NMR(δppm, DMSO-d_6) 7.99 (3H, brs), 7.84 (2H, d, J=7.9Hz), 7.54 (2H, d, J=8.3Hz), 4.77-4.74 (0.42H, m), 4.52-4.49 (0.58H, m), 4.26 (0.58H, brs), 4.11 (0.42H, brs), 3.74 (2H, s), 3.21 (2H, d, J=6.4Hz), 2.96 (1.26H, s), 2.88 (1.74H, s), 2.23-2.04 (4H, m), 1.89-1.86 (2H, m), 1.62-1.59 (6H, m), 1.20-1.07 (4H, m).
Example 287		^{1}H-NMR(δppm, DMSO-d_6) 8.00 (3H, brs), 7.80-7.78 (2H, m), 7.61-7.59 (2H, m), 4.77-4.74 (0.41H, m), 4.53-4.51 (0.59H, m), 4.26 (0.59H, d, J=4.9Hz), 4.12 (0.41H, d, J=4.9Hz), 3.75 (2H, s), 3.20 (2H, d, J=5.7Hz), 2.96 (1.23H, s), 2.88 (1.77H, s), 2.22-2.05 (4H, m), 1.88-1.85 (2H, m), 1.66-1.55 (6H, m), 1.20-1.01 (4H, m).
Example 288		^{1}H-NMR(δppm, DMSO-d_6) 9.96 (1H, s), 8.09 (1H, d, J=2.3Hz), 8.00 (3H, brs), 7.66 (1H, d, J=8.7Hz), 7.20 (1H, d, J=8.3Hz), 4.79-4.76 (0.42H, m), 4.56-4.53 (0.58H, m), 4.30 (0.58H, brs), 4.17 (0.42H, brs), 2.98 (1.26H, s), 2.89 (1.74H, s), 2.44 (3H, s), 2.32-1.95 (6H, m), 1.76-1.63 (6H, m), 1.14-1.02 (4H, m).

Table 1-81

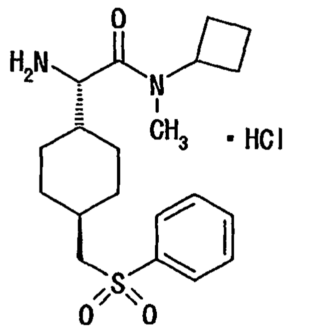
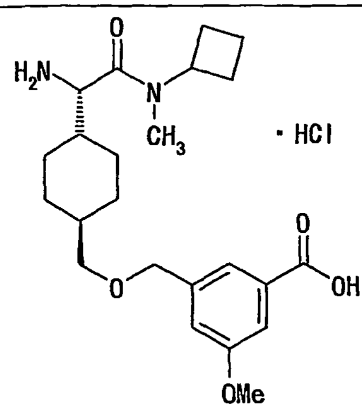
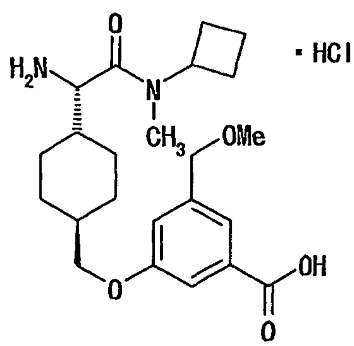
Example 289		^{1}H-NMR(δppm, DMSO-d_6) 7.98 (3H, brs), 7.90 (2H, d, J=7.2Hz), 7.76 (1H, t, J=7.3Hz), 7.66 (2H, t, J=7.3Hz), 4.77-4.74 (0.43H, m), 4.52-4.48 (0.57H, m), 4.26 (0.57H, d, J=3.8Hz), 4.12 (0.43H, d, J=4.5Hz), 3.22 (2H, d, J=5.7Hz), 2.96 (1.28H, s), 2.88 (1.72H, s), 2.23-2.09 (4H, m), 1.87-1.84 (2H, m), 1.62-1.58 (6H, m), 1.15-1.05 (4H, m).
Example 290		^{1}H-NMR(δppm, DMSO-d_6) 8.00 (3H, brs), 7.48 (1H, s), 7.35 (1H, s), 7.10 (1H, s), 4.79-4.76 (0.42H, m), 4.53-4.47 (0.58H, m), 4.50 (2H, s), 4.29 (0.58H, d, J=4.5Hz), 4.15 (0.42H, d, J=5.3Hz), 3.80 (3H, s), 3.24 (2H, d, J=6.0Hz), 2.98 (1.27H, s), 2.89 (1.73H, s), 2.23-2.09 (4H, m), 1.82-1.48 (8H, m), 1.18-1.07 (2H, m), 0.93-0.89 (2H, m).
Example 291		^{1}H-NMR(δppm, DMSO-d_6) 7.99 (3H, brs), 7.46 (1H, s), 7.31 (1H, s), 7.08 (1H, s), 4.79-4.76 (0.43H, m), 4.55-4.52 (0.57H, m), 4.42 (2H, s), 4.31 (0.57H, d, J=5.1Hz), 4.17 (0.43H, d, J=3.7Hz), 3.82 (2H, d, J=6.0Hz), 3.29 (3H, s), 2.98 (1.28H, s), 2.89 (1.72H, s), 2.26-2.13 (4H, m), 1.89-1.87 (2H, m), 1.66-1.64 (6H, m), 1.22-1.02 (4H, m).

Table 1-82

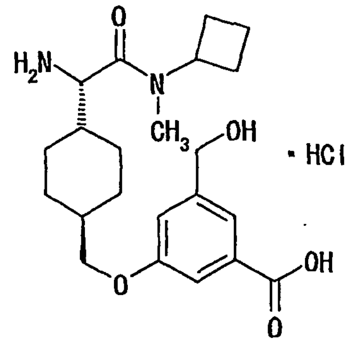
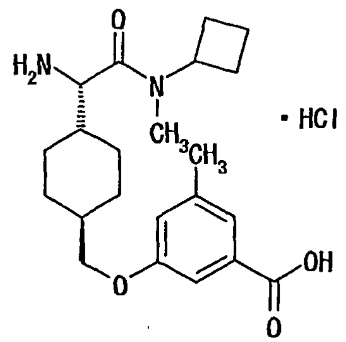
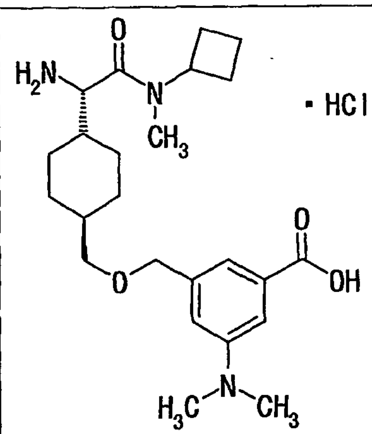
Example 292		^{1}H-NMR(δppm, DMSO-d_6) 8.06 (3H, brs), 7.48 (1H, s), 7.26 (1H, s), 7.09 (1H, s), 5.30 (1H, t, J=5.8Hz), 4.77-4.75 (0.43H, m), 4.55-4.50 (0.57H, m), 4.50 (2H, d, J=5.6Hz), 4.30 (0.57H, d, J=5.6Hz), 4.15 (0.43H, d, J=5.1Hz), 3.80 (2H, d, J=6.0Hz), 2.98 (1.30H, s), 2.89 (1.70H, s), 2.32-2.05 (4H, m), 1.89-1.86 (2H, m), 1.66-1.64 (6H, m), 1.26-0.98 (4H, m).
Example 293		^{1}H-NMR(δppm, DMSO-d_6) 8.04 (3H, brs), 7.33 (1H, s), 7.20 (1H, s), 6.98 (1H, s), 4.78-4.76 (0.43H, m), 4.54-4.52 (0.57H, m), 4.30 (0.57H, d, J=5.1Hz), 4.15 (0.43H, d, J=5.1Hz), 3.79 (2H, d, J=6.5Hz), 2.98 (1.29H, s), 2.89 (1.71H, s), 2.35-2.04 (4H, m), 2.31 (3H, s), 1.88-1.86 (2H, m), 1.65-1.63 (6H, m), 1.26-0.97 (4H, m).
Example 294		^{1}H-NMR(δppm, DMSO-d_6) 8.05(3H, brs), 7.26(2H, brs), 6.97(1H, brs), 4.76-4.74(0.44H, m), 4.52-4.50(0.56H, m), 4.43(2H, s), 4.28(0.56H, brs), 4.13(0.44H, brs), 3.22(2H, d, J=6.5Hz), 2.96(1.31H, s), 2.94(6H, s), 2.87(1.69H, s), 2.31-1.93(4H, m), 1.79-1.76(2H, m), 1.64-1.46(6H, m), 1.12-0.95(4H, m).

Table 1-83

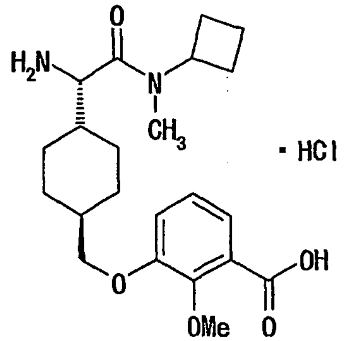
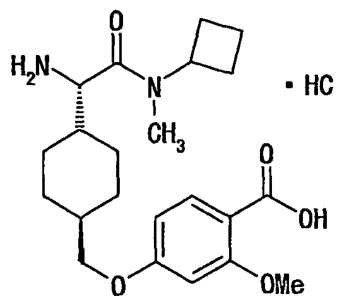
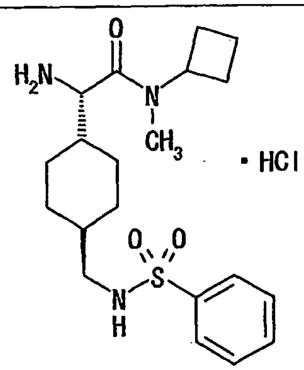
Example 295		^{1}H-NMR(δppm, DMSO-d_6) 8.07 (3H, brs), 7.17-7.12 (2H, m), 7.07 (1H, t, J=7.9Hz), 4.81-4.72 (0.42H, m), 4.56-4.54 (0.58H, m), 4.30 (0.58H, d, J=5.1Hz), 4.15 (0.42H, d, J=5.1Hz), 3.81 (2H, d, J=5.6Hz), 3.75 (3H, s), 2.98 (1.25H, s), 2.89 (1.75H, s), 2.31-1.97 (4H, m), 1.90-1.88 (2H, m), 1.64-1.62 (6H, m), 1.19-1.10 (4H, m).
Example 296		^{1}H-NMR(δppm, DMSO-d_6) 8.06 (3H, s), 7.67 (1H, d, J=8.3Hz), 6.56 (1H, d, J=1.9Hz), 6.53 (1H, dd, J=8.6, 2.1Hz), 4.77-4.75 (0.43H, m), 4.54-4.52 (0.57H, m), 4.31 (0.57H, brs), 4.16 (0.43H, brs), 3.83 (2H, d, J=6.0Hz), 3.78 (3H, s), 2.98 (1.29H, s), 2.89 (1.71H, s), 2.24-2.05 (4H, m), 1.88-1.86 (2H, m), 1.65-1.58 (6H, m), 1.22-0.97 (4H, m).
Example 298		^{1}H-NMR(δppm, DMSO-d_6) 0.75-0.79 (2H, m), 1.05-1.21 (3H, m), 1.62-1.65 (7H, m), 1.91-2.30 (4H, m), 2.56 (2H, d, J=5.65Hz), 2.88 (1.65H, s), 2.96 (1.35H, s), 4.11-4.15 (0.45H, m), 4.26-4.29 (0.55H, m), 4.51-4.54 (0.55H, m), 4.74-4.77 (0.45H, m), 7.59-7.61 (4H, m), 7.78 (2H, d, J=6.78Hz), 8.07 (3H, brs).

Table 1−84

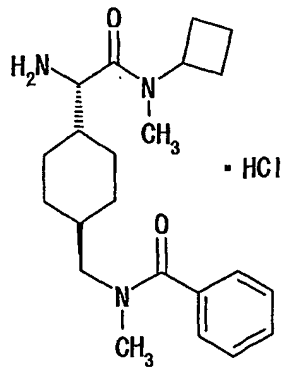
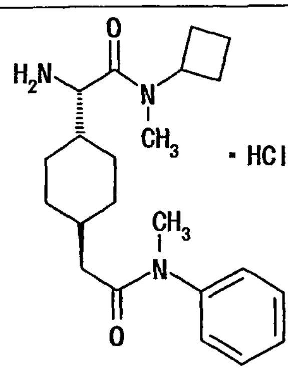
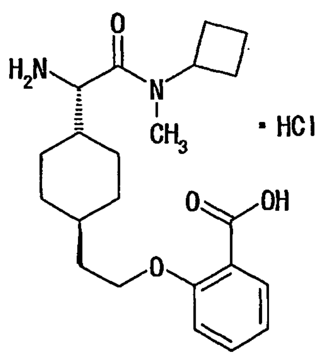
Example 299		^{1}H-NMR(δppm, DMSO-d_6) 0.46-0.62 (1H, m), 0.97-1.16 (3H, m), 1.42-1.84 (8H, m), 1.98-2.31 (4H, m), 2.88-3.02 (6H, m), 3.25-3.31 (2H, m), 4.07-4.35 (1H, m), 4.46-4.59 (0.55H, m), 4.70-4.81 (0.45H, m), 7.32-7.42 (5H, m), 8.12 (3H, brs).
Example 300		^{1}H-NMR(δppm, DMSO-d_6) 0.60-0.78 (2H, m), 1.01-1.25 (3H, m), 1.45-1.72 (8H, m), 1.82-2.32 (6H, m), 2.87 (1.65H, s), 2.95 (1.35H, s), 3.15 (3H, s), 4.08-4.10 (0.45H, m), 4.24-4.26 (0.55H, m), 4.45-4.54 (0.55H, m), 4.69-4.80 (0.45H, m), 7.20-7.53 (5H, m), 8.12 (3H, brs).
Example 301		^{1}H-NMR(δppm, DMSO-d_6) 0.83-1.28 (4H, m), 1.34-1.49 (1H, m), 1.53-1.89 (9H, m), 1.96-2.37 (4H, m), 2.89 (1.65H, s), 2.98 (1.35H, s), 3.99-4.19 (2.45H, m), 4.25-4.35 (0.55H, m), 4.48-4.60 (0.55H, m), 4.70-4.83 (0.45H, m), 6.97 (1H, t, J=7.40Hz), 7.11 (1H, d, J=7.40Hz), 7.46 (1H, t, J=7.40Hz), 7.59 (1H, d, J=7.40Hz), 8.10 (3H, brs).

Table 1-85

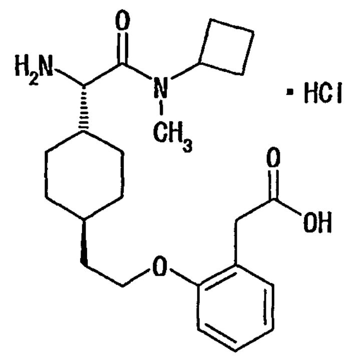
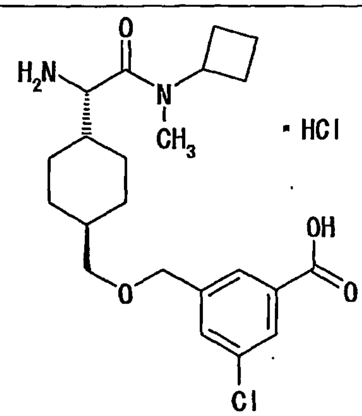
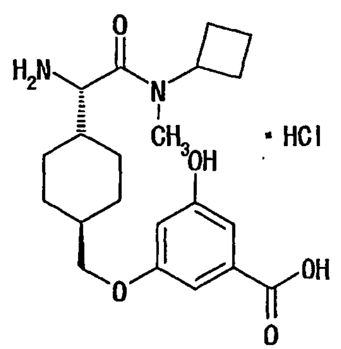
Example 302		^{1}H-NMR(δppm, DMSO-d_6) 0.85-1.00 (2H, m), 1.06-1.26 (2H, m), 1.31-1.47 (1H, m), 1.54-1.86 (11H, m), 1.98-2.36 (4H, m), 2.89 (1.65H, s), 3.00 (1.35H, s), 3.59 (2H, d, J=6.13Hz), 3.60 (2H, s), 3.97 (2H, t, J=6.13Hz), 4.14-4.17 (0.45H, m), 4.30-4.33 (0.55H, m), 4.50-4.61 (0.55H, m), 4.71-4.84 (0.45H, m), 6.88 (1H, t, J=7.35Hz), 6.96 (1H, d, J=8.29Hz), 7.15-7.28 (2H, m), 8.15 (3H, brs).
Example 303		^{1}H-NMR(δppm, DMSO-d_6) 0.86-1.00 (2H, m), 1.06-1.25 (2H, m), 1.44-1.85 (8H, m), 1.97-2.34 (4H, m), 2.89 (1.65H, s), 2.98 (1.35H, s), 3.26 (2H, d, J=6.03Hz), 4.12-4.18 (0.45H, m), 4.27-4.33 (0.55H, m), 4.50-4.57 (2.55H, m), 4.70-4.82 (0.45H, m), 7.61 (1H, s), 7.80 (1H, s), 7.83 (1H, s), 8.05 (3H, brs).
Example 304		^{1}H-NMR(δppm, DMSO-d_6) 0.96-1.26 (4H, m), 1.57-1.75 (6H, m), 1.82-1.91 (2H, m), 1.97-2.36 (4H, m), 2.90 (1.65H, s), 2.99 (1.35H, s), 3.76 (2H, d, J=5.10Hz), 4.15-4.18 (0.45H, m), 4.30-4.33 (0.55H, m), 4.50-4.59 (0.45H, m), 4.73-4.82 (0.55H, m), 6.53 (1H, s), 6.88 (1H, s), 6.95 (1H, s), 8.09 (3H, brs), 9.80 (1H, s), 12.83 (1H, brs).

Table 1-86

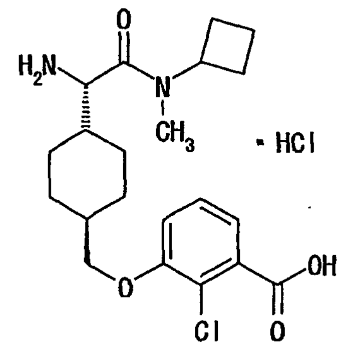
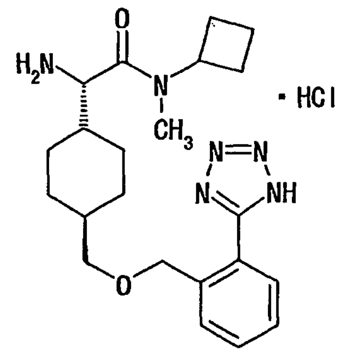
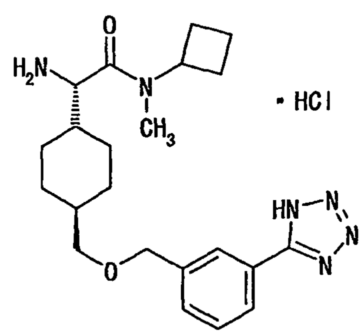
Example 305		^{1}H-NMR(δppm, DMSO-d_6) 1.02-1.29 (4H, m), 1.59-1.76 (6H, m), 1.87-1.94 (2H, m), 1.97-2.35 (4H, m), 2.90 (1.65H, s), 2.99 (1.35H, s), 3.90 (2H, d, J=5.57Hz), 4.15-4.18 (0.45H, m), 4.30-4.33 (0.55H, m), 4.50-4.59 (0.55H, m), 4.74-4.82 (0.45H, m), 7.25 (1H, dd, J=7.42, 2.78Hz), 7.25 (1H, dd, J=7.42, 2.78Hz), 7.34 (1H, t, J=7.42Hz), 8.08 (3H, brs), 13.34 (1H, brs).
Example 306		^{1}H-NMR(δppm, DMSO-d_6) 0.72-0.87 (2H, m), 1.02-1.22 (1H, m), 1.31-1.40 (1H, m), 1.52-1.69 (8H, m), 1.96-2.33 (4H, m), 2.88 (1.65H, s), 2.97 (1.35H, s), 3.17 (2H, d, J=6.49Hz), 4.11-4.13 (0.45H, m), 4.26-4.28 (0.55H, m), 4.48-4.56 (0.55H, m), 4.73-4.79 (2.45H, m), 7.50 (1H, t, J=7.65Hz), 7.59 (1H, t, J=7.65Hz), 7.64 (1H, d, J=7.65Hz), 7.76 (1H, d, J=7.65Hz), 8.10 (3H, brs).
Example 307		^{1}H-NMR(δppm, DMSO-d_6) 0.86-1.00 (2H, m), 1.07-1.27 (2H, m), 1.47-1.71 (6H, m), 1.78-1.86 (2H, m), 1.97-2.33 (4H, m), 2.89 (1.65H, s), 2.98 (1.35H, s), 3.29 (2H, d, J=6.03Hz), 4.13-4.15 (0.45H, m), 4.28-4.30 (0.55H, m), 4.52-4.56 (2.55H, m), 4.72-4.81 (0.45H, m), 7.51 (1H, d, J=7.42Hz), 7.58 (1H, t, J=7.65Hz), 8.02 (1H, d, J=7.88Hz), 8.06 (1H, s), 8.13 (2H, brs).

Table 1-87

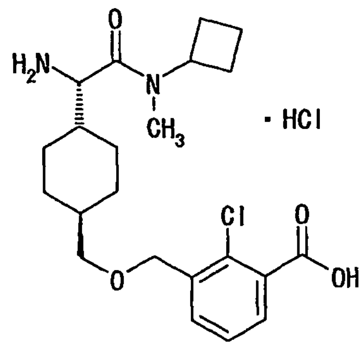
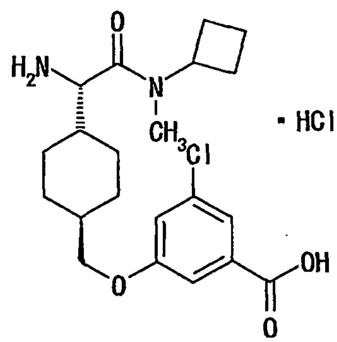
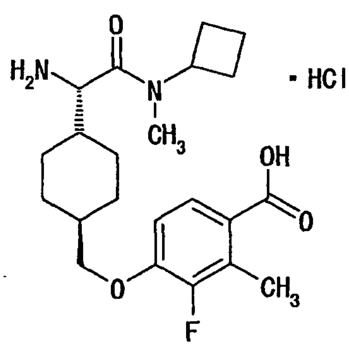
Example 308		^{1}H-NMR(δppm, DMSO-d_6) 0.86-1.00 (2H, m), 1.08-1.28 (2H, m), 1.47-1.72 (6H, m), 1.77-1.85 (2H, m), 1.95-2.20 (3H, m), 2.23-2.33 (1H, m), 2.88 (1.65H, s), 2.98 (1.35H, s), 3.32 (2H, d, J=6.49Hz), 4.12-4.14 (0.45H, m), 4.27-4.30 (0.55H, m), 4.52-4.56 (2.55H, m), 4.71-4.80 (0.45H, m), 7.43 (1H, t, J=7.65Hz), 7.61 (1H, d, J=7.88Hz), 7.64 (1H, dd, J=7.65, 1.62Hz), 8.16 (3H, brs), 13.41 (1H, brs).
Example 309		^{1}H-NMR(δppm, DMSO-d_6) 0.95-1.31 (4H, m), 1.58-1.75 (7H, m), 1.84-1.91 (2H, m), 1.98-2.21 (2H, m), 2.23-2.34 (1H, m), 2.90 (1.65H, s), 2.99 (1.35H, s), 3.86 (2H, d, J=6.03Hz), 4.14-4.16 (0.45H, m), 4.29-4.32 (0.55H, m), 4.51-4.59 (0.55H, m), 4.73-4.82 (0.45H, m), 7.28 (1H, s), 7.36 (1H, s), 7.46 (1H, s), 8.15 (3H, brs), 13.35 (1H, brs).
Example 310		^{1}H-NMR(δppm, DMSO-d_6) 0.96-1.30 (4H, m), 1.58-1.76 (6H, m), 1.83-1.91 (2H, m), 1.98-2.21 (3H, m), 2.23-2.34 (1H, m), 2.43 (3H, d, J=2.32Hz), 2.90 (1.65H, s), 2.99 (1.35H, s), 3.91 (2H, d, J=6.49Hz), 4.14-4.17 (0.45H, m), 4.29-4.32 (0.55H, m), 4.51-4.59 (0.55H, m), 4.73-4.81 (0.45H, m), 7.05 (1H, t, J=8.58Hz), 7.68 (1H, dd, J=8.58, 2.32Hz), 8.14 (3H, brs), 12.73 (1H, brs).

Table 1—88

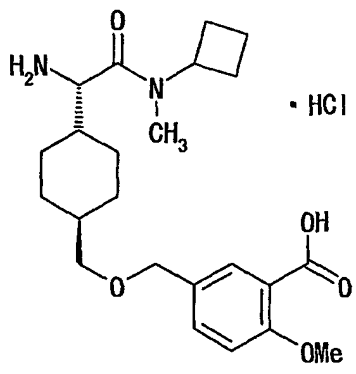
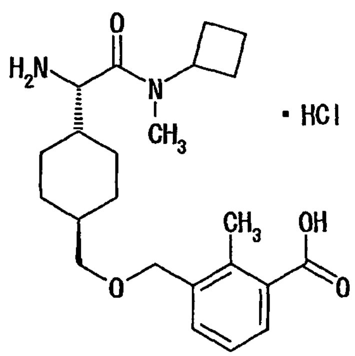
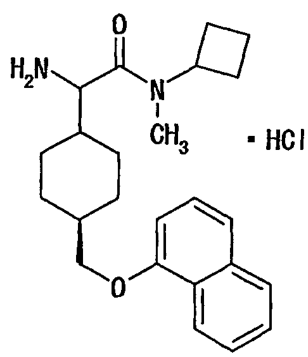
Example 311		^{1}H-NMR(δppm, DMSO-d_6) 0.82-0.97 (2H, m), 1.05-1.29 (2H, m), 1.40-1.50 (1H, m), 1.56-1.81 (7H, m), 1.95-2.33 (4H, m), 2.88 (1.65H, s), 2.97 (1.35H, s), 3.20 (2H, d, J=7.42Hz), 3.81 (3H, s), 4.11-4.14 (0.45H, m), 4.26-4.29 (0.55H, m), 4.38 (2H, s), 4.49-4.57 (0.55H, m), 4.71-4.80 (0.45H, m), 7.09 (1H, d, J=8.35Hz), 7.43 (1H, dd, J=8.35, 1.86Hz), 7.57 (1H, d, J=1.86Hz), 8.15 (3H, brs), 12.59 (1H, brs).
Example 312		^{1}H-NMR(δppm, DMSO-d_6) 0.85-1.00 (2H, m), 1.06-1.26 (2H, m), 1.43-1.52 (1H, m), 1.57-1.70 (5H, m), 1.75-1.83 (2H, m), 1.96-2.33 (4H, m), 2.41 (3H, s), 2.88 (1.65H, s), 2.98 (1.35H, s), 3.26 (2H, d, J=6.03Hz), 4.12-4.14 (0.45H, m), 4.27-4.29 (0.55H, m), 4.47 (3H, s), 4.50-4.57 (0.55H, m), 4.71-4.80 (0.45H, m), 7.24 (1.08H, t, J=7.65Hz), 7.46 (1.06H, d, J=7.42Hz), 7.63 (1H, d, J=7.88Hz), 8.11 (3H, brs), 12.86 (1H, brs).
Example 313		^{1}H-NMR(δppm, DMSO-d_6) 1.08-1.39 (4H, m), 1.59-1.89 (6H, m), 1.96-2.37 (6H, m), 2.90 (1.74H, s), 3.02 (1.26H, s), 3.97 (2H, d, J=6.0Hz), 4.18 (0.42H, d, J=5.1Hz), 4.33 (0.58H, d, J=5.6Hz), 4.52-4.63 (0.58H, m), 4.72-4.87 (0.42H, m), 6.93 (1H, d, J=7.4Hz), 7.35-7.59 (4H, m), 7.86 (1H, dd, J=7.2, 2.1Hz), 8.07 (3H, brs), 8.15 (1H, d, J=7.9Hz).

Table 1—89

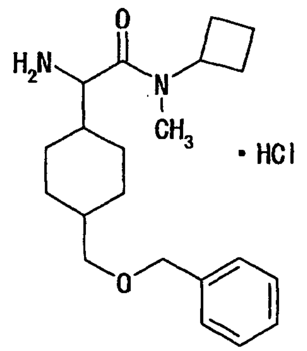
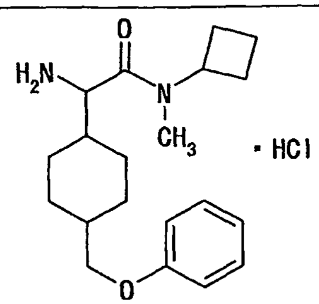
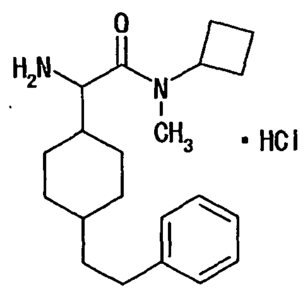
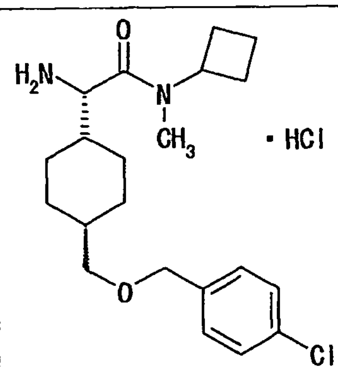
Example 314		^{1}H-NMR(δppm, DMSO-d_6) 0.83-1.27 (4H, m), 1.43-1.52 (1H, m), 1.55-1.72 (5H, m), 1.75-1.84 (2H, m), 1.97-2.22 (3H, m), 2.22-2.35 (1H, m), 2.89 (1.74H, s), 2.98 (1.26H, s), 3.23 (2H, d, J=6.5Hz), 4.13 (0.42H, d, J=5.1Hz), 4.28 (0.58H, d, J=5.1Hz), 4.43 (2H, s), 4.49-4.59 (0.58H, m), 4.72-4.83 (0.42H, m), 7.25-7.36 (5H, m), 7.98 (3H, brs).
Example 315		^{1}H-NMR(δppm, DMSO-d_6) 0.98-1.27 (4H, m), 1.58-1.73 (6H, m), 1.82-1.96 (2H, m), 1.96-2.38 (4H, m), 2.90 (1.74H, s), 2.99 (1.26H, s), 3.77 (2H, d, J=6.5Hz), 4.16 (0.42H, d, J=5.1Hz), 4.30 (0.58H, d, J=5.1Hz), 4.50-4.59 (0.58H, m), 4.72-4.82 (0.42H, m), 6.86-6.95 (3H, m), 7.27 (2H, t, J=7.9Hz), 8.00 (3H, brs).
Example 316		^{1}H-NMR(δppm, DMSO-d_6) 0.79-1.23 (4H, m), 1.41-1.48 (2H, m), 1.54-1.71 (6H, m), 1.74-1.85 (2H, m), 1.96-2.33 (4H, m), 2.57 (2H, t, J=7.9Hz), 2.88 (1.74H, s), 2.97 (1.26H, s), 4.12 (0.42H, d, J=5.6Hz), 4.27 (0.58H, d, J=5.6Hz), 4.47-4.57 (0.58H, m), 4.73-4.79 (0.42H, m), 7.13-7.17 (3H, m), 7.25 (2H, t, J=7.4Hz), 7.99 (3H, brs).
Example 317		^{1}H-NMR(δppm, DMSO-d_6) 0.81-1.30 (4H, m), 1.43-1.52 (1H, m), 1.53-1.72 (5H, m), 1.73-1.83 (2H, m), 1.95-2.36 (4H, m), 2.88 (1.74H, s), 2.98 (1.26H, s), 3.22 (2H, d, J=6.5Hz), 4.14 (0.42H, d, J=5.6Hz), 4.29 (0.58H, d, J=5.6Hz), 4.44 (2H, s), 4.49-4.59 (0.58H, m), 4.71-4.83 (0.42H, m), 7.32 (2H, d, J=8.3Hz), 7.40 (2H, d, J=8.3Hz), 8.02 (3H, s).

Table 1—90

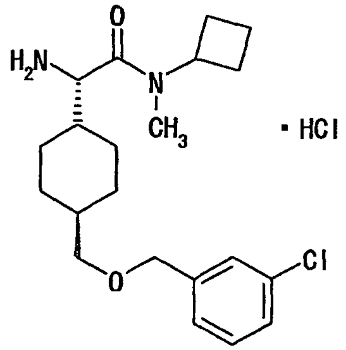
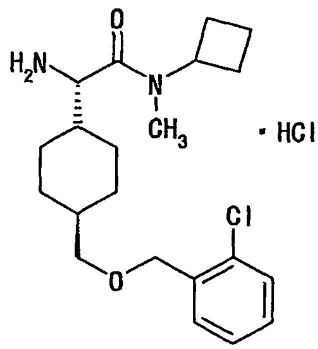
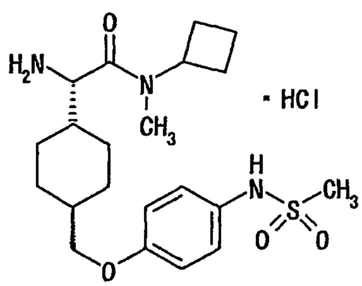
Example 318		^{1}H-NMR(δppm, DMSO-d_6) 0.83-1.29 (4H, m), 1.42-1.54 (1H, m), 1.54-1.74 (5H, m), 1.73-1.86 (2H, m), 1.96-2.35 (4H, m), 2.89 (1.74H, s), 2.98 (1.26H, s), 3.24 (2H, d, J=6.0Hz), 4.14 (0.42H, d, J=5.1Hz), 4.29 (0.58H, d, J=5.1Hz), 4.45 (2H, s), 4.49-4.57 (0.58H, m), 4.71-4.84 (0.42H, m), 7.24-7.41 (4H, m), 8.00 (3H, brs).
Example 319		^{1}H-NMR(δppm, DMSO-d_6) 0.84-1.28 (3H, m), 1.44-1.55 (1H, m), 1.58-1.74 (4H, m), 1.76-1.85 (2H, m), 1.98-2.36 (4H, m), 2.89 (1.74H, s), 2.98 (1.26H, s), 3.30 (2H, d, J=6.0Hz), 3.33 (3H, s), 4.14 (0.42H, d, J=5.6Hz), 4.29 (0.58H, d, J=5.6Hz), 4.51 (2H, s), 4.51-4.58 (0.58H, m), 4.74-4.84 (0.42H, m), 7.29-7.39 (2H, m), 7.40-7.50 (2H, m), 8.00 (3H, s).
Example 320		^{1}H-NMR(δppm, DMSO-d_6) 0.92-1.31 (4H, m), 1.56-1.82 (6H, m), 1.83-1.94 (2H, m), 1.96-2.37 (4H, m), 2.87 (3H, s), 2.90 (1.74H, s), 2.99 (1.26H, s), 3.74 (2H, d, J=6.5Hz), 4.16 (0.42H, d, J=5.1Hz), 4.31 (0.58H, d, J=5.1Hz), 4.48-4.61 (0.58H, m), 4.70-4.84 (0.42H, m), 6.88 (2H, d, J=8.8Hz), 7.12 (2H, d, J=8.8Hz), 7.98 (3H, brs), 9.35 (1H, brs).

Table 1−91

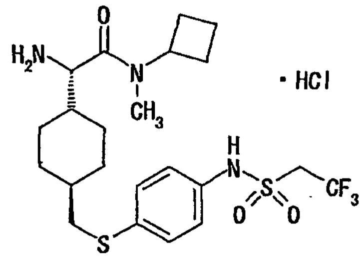
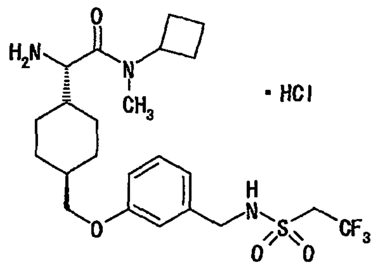
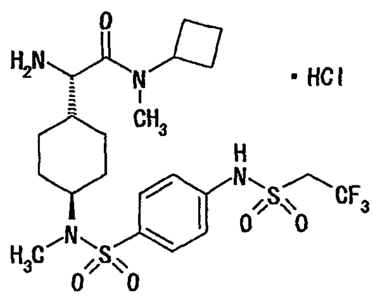
Example 321		^{1}H-NMR(δppm, DMSO-d_6) 0.85-1.26 (4H, m), 1.30-1.40 (1H, m), 1.53-1.74 (5H, m), 1.86-2.35 (6H, m), 2.81 (2H, d, J=7.0Hz), 2.88 (1.74H, s), 2.96 (1.26H, s), 4.11 (0.42H, d, J=5.1Hz), 4.26 (0.58H, d, J=5.1Hz), 4.44-4.60 (2.58H, m), 4.71-4.85 (0.42H, m), 7.15 (2H, d, J=8.8Hz), 7.29 (2H, d, J=8.8Hz), 8.14 (3H, brs).
Example 322		^{1}H-NMR(δppm, DMSO-d_6) 0.67-1.22 (4H, m), 1.41-1.71 (8H, m), 1.96-2.33 (4H, m), 2.85 (1.74H, s), 2.92 (1.26H, s), 3.00 (2H, d, J=7.0Hz), 4.02-4.56 (5.58H, m), 4.65-4.80 (0.42H, m), 6.67 (1H, d, J=7.9Hz), 6.76 (1H, d, J=7.9Hz), 6.80 (1H, s), 7.12 (1H, t, J=7.9Hz), 7.92 (3H, brs), 9.45 (1H, s).
Example 323		^{1}H-NMR(δppm, DMSO-d_6) 1.10-1.46 (4H, m), 1.48-1.70 (5H, m), 1.94-2.37 (6H, m), 2.65 (3H, s), 2.87 (1.74H, s), 2.95 (1.26H, s), 3.50-3.60 (1H, m), 4.12 (0.42H, d, J=4.6Hz), 4.27 (0.58H, d, J=4.6Hz), 4.42-4.55 (0.58H, m), 4.62-4.81 (2.42H, m), 7.35 (2H, d, J=8.8Hz), 7.72 (2H, d, J=8.8Hz), 8.01 (3H, brs), 11.10 (1H, brs).

Table 1—92

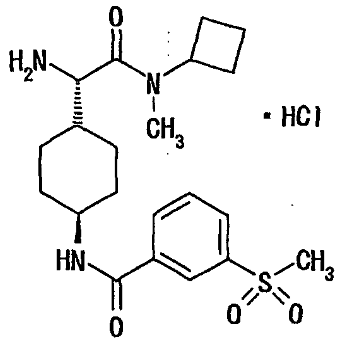
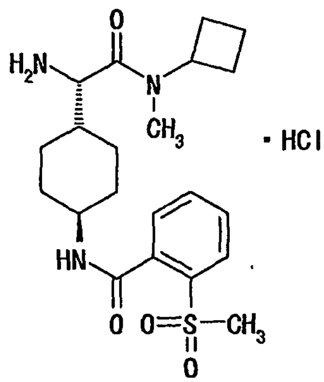
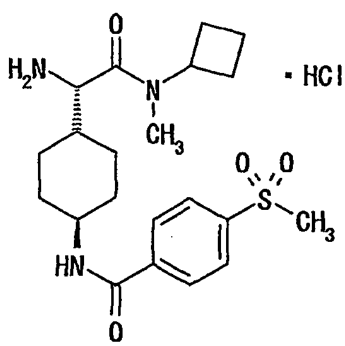
Example 324		^{1}H-NMR(δppm, DMSO-d_6) 1.22-1.39 (4H, m), 1.56-1.79 (5H, m), 1.87-2.35 (6H, m), 2.90 (1.74H, s), 3.00 (1.26H, s), 3.26 (3H, s), 3.67-3.79 (1H, m), 4.17 (0.42H, d, J=5.1Hz), 4.32 (0.58H, d, J=5.1Hz), 4.49-4.61 (0.58H, m), 4.71-4.84 (0.42H, m), 7.74 (1H, t, J=8.3Hz), 7.97 (1H, brs), 8.06 (1H, d, J=8.3Hz), 8.16 (1H, d, J=8.3Hz), 8.35 (1H, s), 8.57 (1H, d, J=7.9Hz).
Example 325		^{1}H-NMR(δppm, DMSO-d_6) 1.11-1.37 (4H, m), 1.56-1.78 (5H, m), 1.91-2.35 (6H, m), 2.89 (1.74H, s), 2.99 (1.26H, s), 3.32 (3H, s), 3.56-3.67 (1H, m), 4.16 (0.42H, d, J=6.0Hz), 4.30 (0.58H, d, J=6.0Hz), 4.51-4.59 (0.58H, m), 4.73-4.81 (0.42H, m), 7.47 (1H, dd, J=7.7, 1.2Hz), 7.68 (1H, td, J=7.7, 1.2Hz), 7.76 (1H, t, J=7.7Hz), 7.94 (1H, d, J=7.7Hz), 7.99 (0H, s), 8.48 (1H, t, J=7.9Hz).
Example 326		^{1}H-NMR(δppm, DMSO-d_6) 1.19-1.38 (4H, m), 1.56-1.75 (5H, m), 1.84-1.95 (2H, m), 1.96-2.38 (4H, m), 2.90 (1.74H, s), 3.00 (1.26H, s), 3.25 (3H, s), 3.60-3.79 (1H, m), 4.17 (0.42H, d, J=5.6Hz), 4.32 (0.58H, d, J=5.6Hz), 4.49-4.62 (0.58H, m), 4.70-4.84 (0.42H, m), 8.00 (2H, d, J=8.8Hz), 8.02 (3H, brs), 8.04 (2H, d, J=8.8Hz), 8.52 (1H, d, J=7.9Hz).

Table 1—93

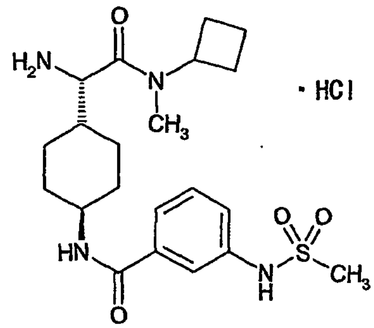
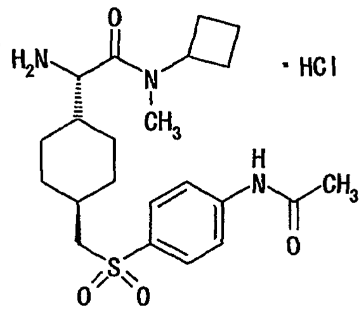
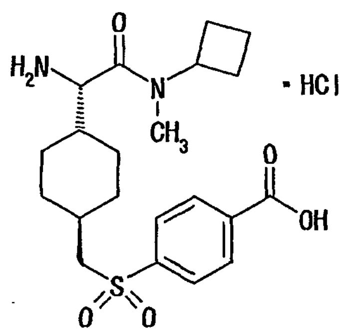
Example 327		^{1}H-NMR(δppm, DMSO-d_6) 1.21-1.38 (4H, m), 1.57-1.74 (6H, m), 1.81-1.93 (2H, m), 2.00-2.35 (4H, m), 2.90 (1.74H, s), 2.99 (3H, s), 3.00 (1.26H, s), 3.62-3.76 (1H, m), 4.16 (0.42H, d, J=5.6Hz), 4.31 (0.58H, d, J=5.6Hz), 4.50-4.60 (0.58H, m), 4.73-4.83 (0.42H, m), 7.30-7.35 (1H, m), 7.39 (1H, t, J=7.7Hz), 7.54 (1H, d, J=7.7Hz), 7.61-7.64 (1H, m), 8.01 (3H, s), 8.25 (1H, d, J=7.9Hz).
Example 328		^{1}H-NMR(δppm, DMSO-d_6) 0.93-1.23 (4H, m), 1.48-1.71 (7H, m), 1.81-1.89 (1H, m), 1.98-2.36 (4H, m), 2.88 (1.74H, s), 2.96 (1.26H, s), 3.15 (2H, d, J=6.0Hz), 4.09 (0.42H, d; J=5.6Hz), 4.23 (0.58H, d, J=5.6Hz), 4.45-4.58 (0.58H, m), 4.70-4.84 (0.42H, m), 7.80 (2H, d, J=9.3Hz), 7.83 (3H, brs), 7.84 (2H, d, J=9.3Hz), 10.47 (1H, brs).
Example 329		^{1}H-NMR(δppm, DMSO-d_6) 0.94-1.23 (4H, m), 1.50-1.72 (7H, m), 1.82-1.90 (1H, m), 1.94-2.37 (4H, m), 2.87 (1.74H, s), 2.95 (1.26H, s), 3.28 (2H, d, J=6.0Hz), 4.09 (0.42H, d, J=4.6Hz), 4.23 (0.58H, d, J=4.6Hz), 4.43-4.55 (0.58H, m), 4.70-4.83 (0.42H, m), 8.00 (2H, d, J=8.3Hz); 8.15 (2H, d, J=8.3Hz).

Table 1−94

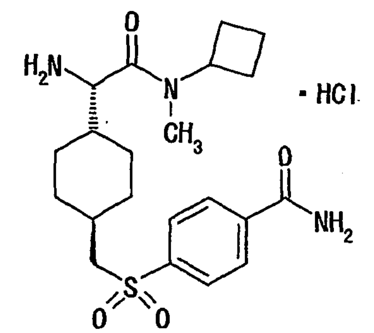
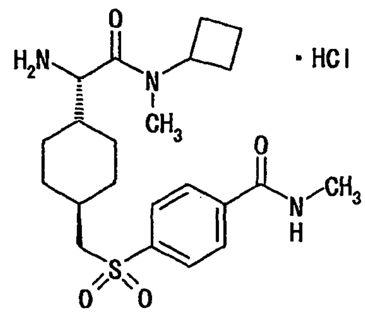
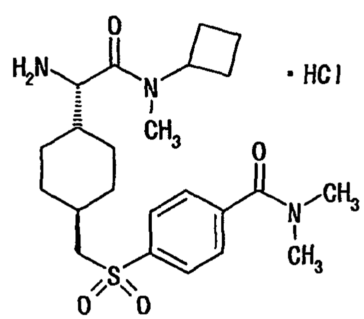
Example 330		^{1}H-NMR(δppm, DMSO-d_6) 0.96-1.22 (4H, m), 1.48-1.71 (7H, m), 1.79-1.91 (1H, m), 1.94-2.35 (4H, m), 2.87 (1.74H, s), 2.95 (1.26H, s), 3.27 (2H, d, J=5.6Hz), 4.08 (0.42H, d, J=5.1Hz), 4.22 (0.58H, d, J=5.1Hz), 4.42-4.58 (0.58H, m), 4.68-4.82 (0.42H, m), 7.67 (1H, brs), 7.90 (3H, brs), 7.97 (2H, d, J=8.3Hz), 8.09 (2H, d, J=8.3Hz), 8.23 (1H, brs).
Example 331		^{1}H-NMR(δppm, DMSO-d_6) 0.93-1.25 (4H, m), 1.47-1.72 (6H, m), 1.80-1.89 (2H, m), 1.93-2.35 (4H, m), 2.80 (3H, d, J=4.6Hz), 2.85 (1.74H, s), 2.95 (1.26H, s), 3.27 (2H, d, J=6.5Hz), 4.09 (0.42H, d, J=5.6Hz), 4.23 (0.58H, d, J=5.6Hz), 4.42-4.57 (0.58H, m), 4.68-4.82 (0.42H, m), 7.97 (3H, brs), 7.98 (2H, d, J=8.3Hz), 8.05 (2H, d, J=8.3Hz), 8.75 (1H, q, J=4.6Hz).
Example 332		^{1}H-NMR(δppm, DMSO-d_6) 0.96-1.21 (4H, m), 1.52-1.76 (6H, m), 1.82-1.91 (2H, m), 1.98-2.37 (4H, m), 2.86 (3H, s), 2.87 (1.74H, s), 2.95 (1.26H, s), 3.00 (3H, s), 3.26 (2H, d, J=6.0Hz), 4.09 (0.42H, d, J=5.6Hz), 4.24 (0.58H, d, J=5.6Hz), 4.41-4.58 (0.58H, m), 4.69-4.85 (0.42H, m), 7.65 (2H, d, J=8.3Hz), 7.93 (3H, brs), 7.94 (2H, d, J=8.3Hz).

Table 1—95

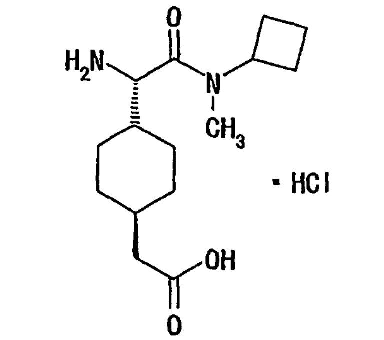
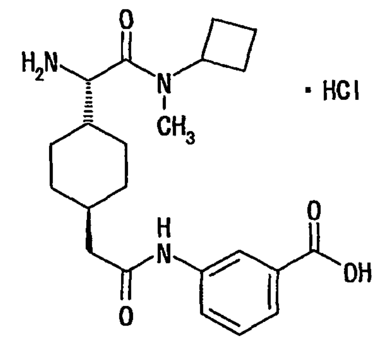
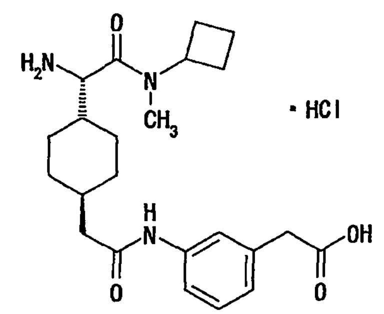
Example 333		^{1}H-NMR(δppm, DMSO-d_6) 0.81-1.31 (4H, m), 1.45-1.80 (6H, m), 1.87-2.36 (6H, m), 2.88 (1.76H, s), 2.97 (1.26H, s), 4.12 (0.42H, d, J=5.1Hz), 4.27 (0.58H, d, J=5.6Hz), 4.43-4.60 (0.58H, m), 4.67-4.85 (0.42H, m), 8.08 (3H, brs).
Example 334		^{1}H-NMR(δppm, DMSO-d_6) 0.84-1.28 (4H, m), 1.52-1.81 (8H, m), 1.93-2.34 (6H, m), 2.88 (1.74H, s), 2.97 (1.26H, s), 4.12 (0.42H, d, J=5.6Hz), 4.27 (0.58H, d, J=5.1Hz), 4.46-4.58 (0.58H, m), 4.70-4.84 (0.42H, m), 7.39 (1H, t, J=7.9Hz), 7.58 (1H, d, J=7.9Hz), 7.79 (1H, d, J=7.9Hz), 8.16 (3H, brs), 8.23 (1H, s), 10.11 (1H, d, J=3.2Hz).
Example 335		^{1}H-NMR(δppm, DMSO-d_6) 0.86-1.28 (4H, m), 1.54-1.84 (8H, m), 1.94-2.36 (6H, m), 2.89 (1.74H, s), 2.98 (1.26H, s), 3.51 (2H, s), 4.13 (0.42H, d, J=4.8Hz), 4.28 (0.58H, d, J=5.5Hz), 4.46-4.60 (0.58H, m), 4.69-4.85 (0.42H, m), 6.91 (1H, d, J=7.9Hz), 7.21 (1H, t, J=7.9Hz), 7.48 (1H, d, J=7.7Hz), 7.49 (1H, s), 8.18 (3H, brs), 9.87 (1H, s).

Table 1-96

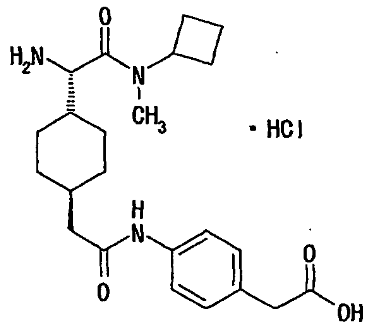
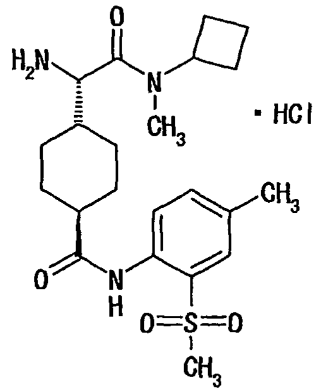
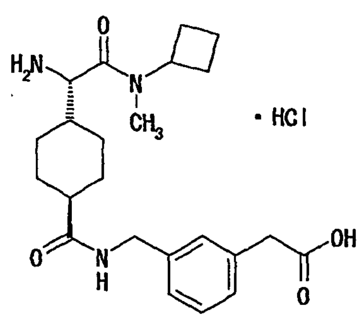
Example 336		^{1}H-NMR(δppm, DMSO-d_6) 0.85-1.28 (4H, m), 1.52-1.79 (8H, m), 1.94-2.33 (6H, m), 2.88 (1.74H, s), 2.96 (1.26H, s), 3.47 (2H, s), 4.12 (0.42H, d, J=5.6Hz), 4.26 (0.58H, d, J=4.6Hz), 4.47-4.57 (0.58H, m), 4.69-4.83 (0.42H, m), 7.14 (2H, d, J=8.8Hz), 7.50 (2H, d, J=8.8Hz), 8.22 (3H, brs), 9.87 (1H, brs).
Example 337		^{1}H-NMR(δppm, DMSO-d_6) 1.14-1.47 (4H, m), 1.58-1.79 (6H, m), 1.96-2.39 (6H, m), 2.36 (3H, s), 2.90 (1.74H, s), 2.99 (1.26H, s), 3.20 (3H, s), 4.17 (0.42H, d, J=5.1Hz), 4.32 (0.58H, d, J=5.6Hz), 4.50-4.63 (0.58H, m), 4.74-4.84 (0.42H, m), 7.51 (1H, d, J=8.8Hz), 7.70 (1H, s), 7.81 (1H, d, J=8.8Hz), 7.99 (3H, brs), 9.52 (1H, s).
Example 338		^{1}H-NMR(δppm, DMSO-d_6) 1.09-1.43 (4H, m), 1.58-1.85 (8H, m), 1.98-2.37 (4H, m), 2.89 (1.74H, s), 2.98 (1.26H, s), 3.52 (2H, s), 4.17 (0.42H, d, J=4.6Hz), 4.21 (2H, d, J=6.0Hz), 4.32 (0.58H, d, J=5.1Hz), 4.48-4.59 (0.58H, m), 4.71-4.82 (0.42H, m), 7.05-7.14 (3H, m), 7.24 (1H, t, J=7.9Hz), 8.07 (3H, brs), 8.28 (1H, t, J=6.0Hz), 12.29 (1H, brs).

Table 1—97

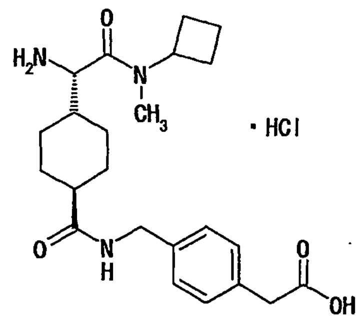
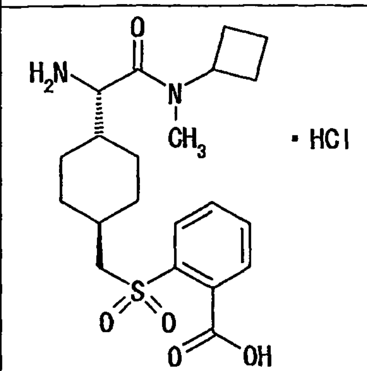
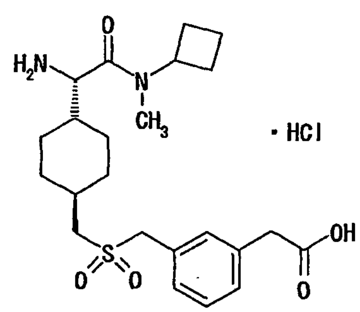
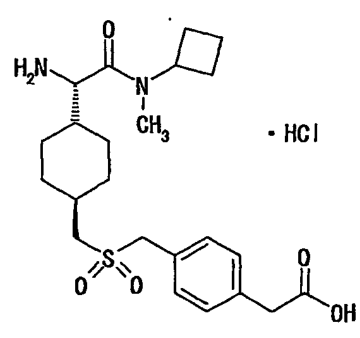
Example 339		^{1}H-NMR(δppm, DMSO-d_6) 1.07-1.42 (4H, m), 1.58-1.85 (8H, m), 1.99-2.35 (4H, m), 2.89 (1.74H, s), 2.98 (1.26H, s), 3.52 (2H, s), 4.11-4.24 (2.42H, m), 4.32 (0.58H, d, J=5.1Hz), 4.49-4.62 (0.58H, m), 4.74-4.85 (0.42H, m), 7.14 (2H, d, J=8.3Hz), 7.18 (2H, d, J=8.3Hz), 8.04 (3H, brs), 8.26 (1H, t, J=5.8Hz), 12.24 (1H, brs).
Example 340		^{1}H-NMR(δppm, DMSO-d_6) 0.98-1.25 (4H, m), 1.48-1.92 (8H, m), 1.96-2.33 (4H, m), 2.88 (1.74H, s), 2.96 (1.26H, s), 3.47 (2H, d, J=6.0Hz), 4.13 (0.42H, d, J=5.1Hz), 4.28 (0.58H, d, J=5.6Hz), 4.45-4.56 (0.58H, m), 4.70-4.82 (0.42H, m), 7.65-7.85 (3H, m), 7.95 (1H, d, J=7.4Hz), 8.02 (3H, brs).
Example 341		^{1}H-NMR(δppm, DMSO-d_6) 0.91-1.28 (4H, m), 1.52-1.95 (8H, m), 1.96-2.35 (4H, m), 2.88 (1.74H, s), 2.93 (2H, d, J=6.0Hz), 2.97 (1.26H, s), 3.57 (2H, s), 4.12 (0.42H, d, J=5.6Hz), 4.27 (0.58H, d, J=5.1Hz), 4.43 (2H, s), 4.47-4.59 (0.58H, m), 4.71-4.82 (0.42H, m), 7.20-7.42 (4H, m), 8.06 (3H, brs).
Example 342		^{1}H-NMR(δppm, DMSO-d_6) 0.96-1.26 (4H, m), 1.54-1.95 (8H, m), 2.00-2.33 (4H, m), 2.88 (1.74H, s), 2.93 (2H, d, J=6.0Hz), 2.97 (1.26H, s), 3.58 (2H, s), 4.13 (0.42H, d, J=5.6Hz), 4.28 (0.58H, d, J=5.1Hz), 4.42 (2H, s), 4.48-4.58 (0.58H, m), 4.71-4.82 (0.42H, m), 7.27 (2H, d, J=8.3Hz), 7.32 (2H, d, J=8.3Hz), 8.04 (3H, brs), 12.24 (1H, brs).

Table 1-98

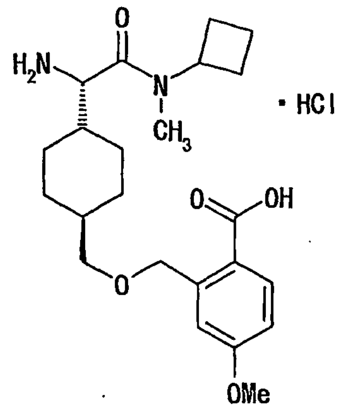
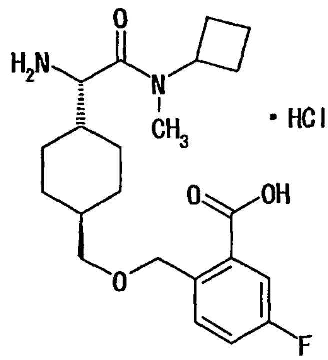
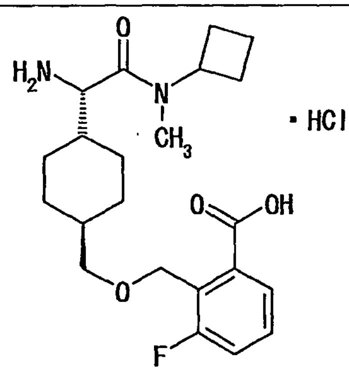
Example 343		^{1}H-NMR(δppm, DMSO-d_6) 0.88-1.31 (4H, m), 1.47-1.70 (6H, m), 1.78-1.87 (2H, m), 1.95-2.35 (4H, m), 2.88 (1.74H, s), 2.98 (1.26H, s), 3.29 (2H, d, J=6.0Hz), 3.56 (1H, s), 4.14 (0.42H, d, J=5.1Hz), 4.28 (0.58H, d, J=5.1Hz), 4.46-4.60 (0.58H, m), 4.69-4.85 (0.42H, m), 4.77 (2H, s), 6.90 (1H, dd, J=8.8, 2.8Hz), 7.11 (1H, d, J=2.8Hz), 7.87 (1H, d, J=8.8Hz), 8.06 (3H, brs).
Example 344		^{1}H-NMR(δppm, DMSO-d_6) 0.83-1.30 (4H, m), 1.43-1.71 (6H, m), 1.85 (2H, m), 1.94-2.33 (4H, m), 2.88 (1.74H, s), 2.97 (1.26H, s), 3.26 (1H, d, J=6.0Hz), 4.13 (0.42H, d, J=5.1Hz), 4.28 (0.58H, d, J=5.1Hz), 4.47-4.59 (0.58H, m), 4.68-4.83 (0.42H, m), 4.71 (2H, s), 7.40 (1H, td, J=8.3, 2.8Hz), 7.54-7.62 (2H, m), 8.05 (3H, brs).
Example 345		^{1}H-NMR(δppm, DMSO-d_6) 0.74-1.24 (4H, m), 1.33-1.43 (1H, m), 1.48-1.80 (7H, m), 1.96-2.37 (4H, m), 2.87 (1.74H, s), 2.95 (1.26H, s), 3.17 (2H, d, J=6.5Hz), 4.11 (0.42H, d, J=4.6Hz), 4.26 (0.52H, d, J=5.1Hz), 4.46-4.56 (0.52H, m), 4.70 (2H, s), 4.72-4.79 (0.42H, m), 7.35-7.55 (3H, m), 7.96 (3H, brs).

Table 1-99

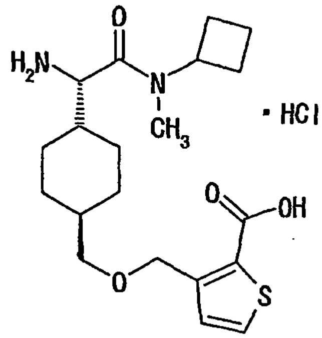
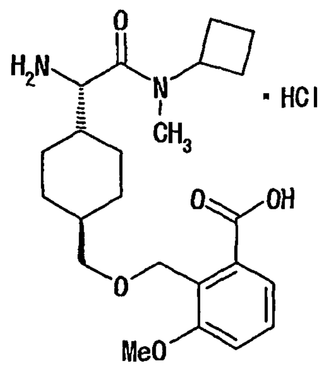
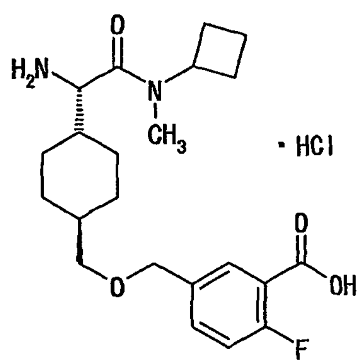
Example 346		^{1}H-NMR(δppm, DMSO-d_6) 0.80-1.29 (4H, m), 1.44-1.85 (8H, m), 1.93-2.35 (4H, m), 2.88 (1.74H, s), 2.97 (1.26H, s), 3.26 (2H, d, J=6.5Hz), 4.14 (0.42H, d, J=5.6Hz), 4.29 (0.58H, d, J=5.6Hz), 4.45-4.57 (0.58H, m), 4.70-4.84 (0.42H, m), 4.74 (2H, s), 7.17 (1H, d, J=5.1Hz), 7.77 (1H, d, J=5.1Hz), 8.01 (3H, brs).
Example 347		^{1}H-NMR(δppm, DMSO-d_6) 0.71-1.25 (4H, m), 1.32-1.44 (1H, m), 1.51-1.80 (7H, m), 1.98-2.35 (4H, m), 2.88 (1.74H, s), 2.96 (1.26H, s), 3.15 (2H, d, J=6.6Hz), 3.80 (3H, s), 4.11 (0.42H, d, J=4.8Hz), 4.26 (0.58H, d, J=4.4Hz), 4.44-4.58 (0.58H, m), 4.66 (2H, s), 4.71-4.83 (0.42H, m), 7.12-7.25 (2H, m), 7.35 (1H, t, J=7.9Hz), 7.99 (3H, brs).
Example 348		^{1}H-NMR(δppm, DMSO-d_6) 0.82-1.29 (4H, m), 1.43-1.85 (8H, m), 1.98-2.35 (4H, m), 2.89 (1.74H, s), 2.97 (1.26H, s), 3.23 (2H, d, J=6.2Hz), 4.13 (0.42H, d, J=4.8Hz), 4.28 (0.58H, d, J=5.1Hz), 4.45 (2H, s), 4.49-4.58 (0.58H, m), 4.69-4.87 (0.42H, m), 7.28 (3H, dd, J=10.6, 8.4Hz), 7.50-7.60 (1H, m), 7.79 (1H, dd, J=7.2, 2.4Hz), 8.09 (3H, s).

Table 1-100

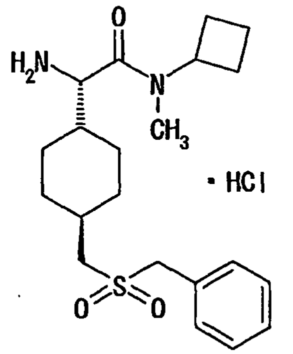
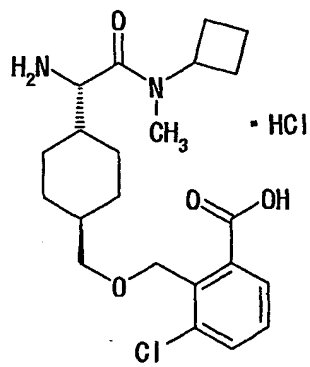
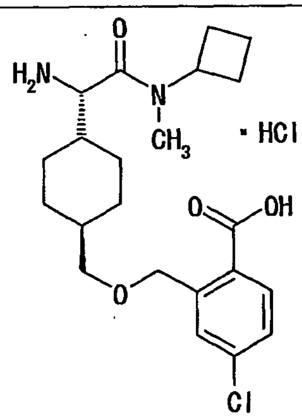
Example 349		^{1}H-NMR(δppm, DMSO-d_6) 0.94-1.28 (4H, m), 1.52-2.36 (12H, m), 2.89 (1.74H, s), 2.94 (2H, d, J=5.9Hz), 2.97 (1.26H, s), 4.12 (0.42H, d, J=5.1Hz), 4.27 (0.58H, d, J=5.5Hz), 4.44-4.60 (0.58H, m), 4.45 (2H, s), 4.68-4.82 (0.42H, m), 7.39 (5H, brs), 8.02 (3H, brs).
Example 350		^{1}H-NMR(δppm, DMSO-d_6) 0.76-1.20 (4H, m), 1.33-1.45 (1H, m), 1.49-1.79 (7H, m), 1.95-2.32 (4H, m), 2.88 (1.74H, s), 2.96 (1.26H, s), 3.19 (2H, d, J=6.0Hz), 4.13 (0.42H, d, J=5.1Hz), 4.28 (0.58H, d, J=4.6Hz), 4.46-4.57 (0.58H, m), 4.72-4.83 (0.42H, m), 4.77 (2H, s), 7.42 (1H, t, J=7.9Hz), 7.60-7.62 (2H, m), 8.01 (3H, brs).
Example 351		^{1}H-NMR(δppm, DMSO-d_6) 0.89-1.28 (4H, m), 1.47-1.86 (8H, m), 1.95-2.36 (4H, m), 2.89 (1.74H, s), 2.98 (1.26H, s), 3.32 (2H, d, J=6.0Hz), 4.14 (0.42H, d, J=5.6Hz), 4.29 (0.58H, d, J=5.6Hz), 4.48-4.59 (0.58H, m), 4.69-4.83 (0.42H, m), 4.77 (2H, s), 7.45 (1H, d, J=8.3Hz), 7.59 (1H, s), 7.86 (1H, d, J=8.3Hz), 7.98 (3H, brs).

Table 1-101

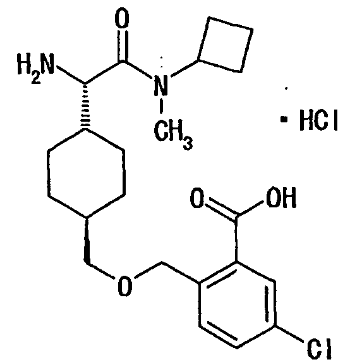
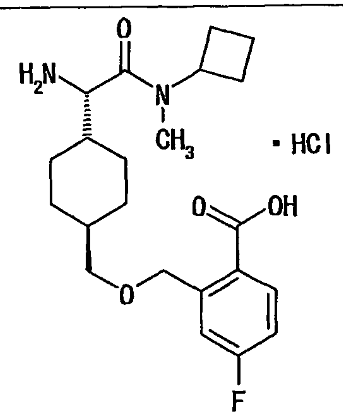
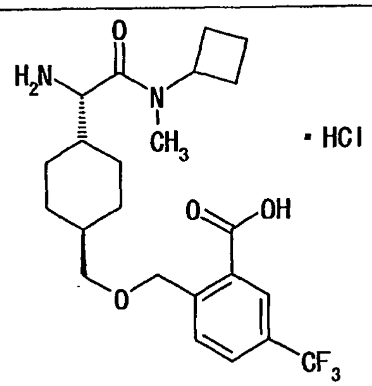
Example 352		^{1}H-NMR(δppm, DMSO-d_6) 0.85-1.25 (4H, m), 1.45-1.85 (8H, m), 1.97-2.34 (4H, m), 2.89 (1.74H, s), 2.98 (1.26H, s), 3.28 (2H, d, J=6.0Hz), 4.14 (0.42H, d, J=5.6Hz), 4.29 (0.58H, d, J=5.6Hz), 4.48-4.59 (0.58H, m), 4.69-4.82 (0.42H, m), 4.73 (2H, s), 7.59 (1H, d, J=8.8Hz), 7.63 (1H, dd, J=8.8, 2.1Hz), 7.79 (1H, d, J=2.1Hz), 8.08 (3H, brs).
Example 353		^{1}H-NMR(δppm, DMSO-d_6) 0.90-1.35 (4H, m), 1.50-1.87 (8H, m), 2.00-2.28 (4H, m), 2.90 (1.74H, s), 2.99 (1.26H, s), 4.15 (0.42H, d, J=5.1Hz), 4.29 (0.58H, d, J=5.1Hz), 4.48-4.62 (0.58H, m), 4.74-4.87 (0.42H, m), 4.79 (2H, s), 7.21 (1H, t, J=8.4Hz), 7.35 (1H, d, J=10.6Hz), 7.95 (1H, dd, J=8.4, 6.1Hz), 8.13 (3H, brs).
Example 354		^{1}H-NMR(δppm, DMSO-d_6) 0.85-1.22 (4H, m), 1.45-1.85 (8H, m), 1.95-2.30 (4H, m), 2.87 (1.74H, s), 2.96 (1.26H, s), 4.15 (0.42H, d, J=5.1Hz), 4.27 (0.58H, d, J=5.1Hz), 4.50-4.60 (0.58H, m), 4.70-4.80 (0.42H, m), 4.82 (2H, s), 7.82 (1H, d, J=8.4Hz), 7.91 (1H, d, J=8.4Hz), 8.00 (3H, brs), 8.07 (1H, s).

Table 1-102

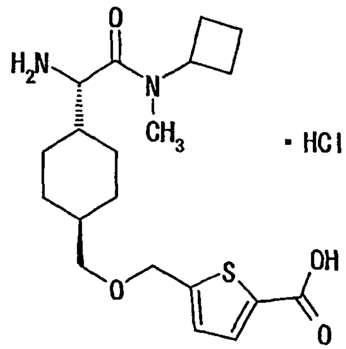
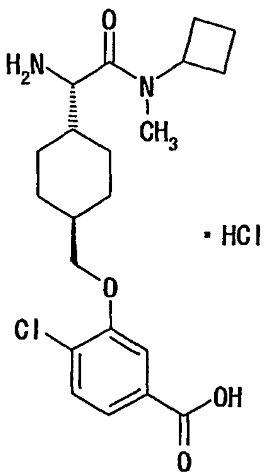
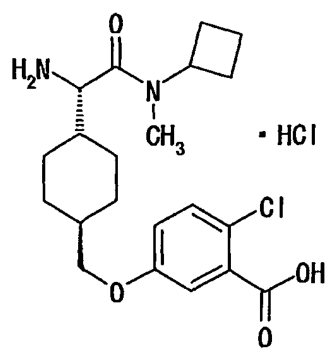
Example 355		^{1}H-NMR(δppm, DMSO-d_6) 0.77-1.23 (4H, m), 1.33-1.79 (8H, m), 1.91-2.29 (4H, m), 2.82 (1.74H, s), 2.91 (1.26H, s), 3.20 (2H, d, J=6.5Hz), 4.07 (0.42H, d, J=5.1Hz), 4.21 (0.58H, d, J=5.6Hz), 4.41-4.50 (0.58H, m), 4.57 (2H, s), 4.65-4.78 (0.42H, m), 6.99 (1H, d, J=3.2Hz), 7.53 (1H, d, J=3.2Hz), 7.98 (3H, brs).
Example 356		^{1}H-NMR(δppm, DMSO-d_6) 1.01-1.29 (4H, m), 1.55-1.77 (6H, m), 1.84-2.35 (6H, m), 2.89 (1.74H, s), 2.98 (1.26H, s), 3.92 (2H, d, J=6.0Hz), 4.15 (0.42H, d, J=5.1Hz), 4.30 (0.58H, d, J=5.1Hz), 4.52-4.55 (0.58H, m), 4.76-4.78 (0.42H, m), 7.47-7.55 (3H, m), 8.05 (3H, brs).
Example 357		^{1}H-NMR(δppm, DMSO-d_6) 0.92-1.28 (4H, m), 1.52-1.76 (6H, m), 1.94-2.35 (6H, m), 2.88 (1.74H, s), 2.97 (1.26H, s), 3.80 (2H, d, J=6.0Hz), 4.16 (0.42H, brs), 4.30 (0.58H, brs), 4.46-4.59 (0.58H, m), 4.71-4.81 (0.42H, m), 7.07 (1H, dd, J=8.8, 2.8Hz), 7.24 (1H, d, J=2.8Hz), 7.40 (1H, d, J=8.8Hz), 8.04 (3H, s).

Table 1-103

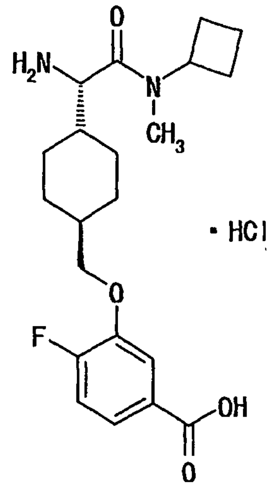
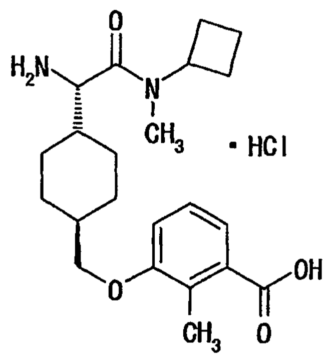
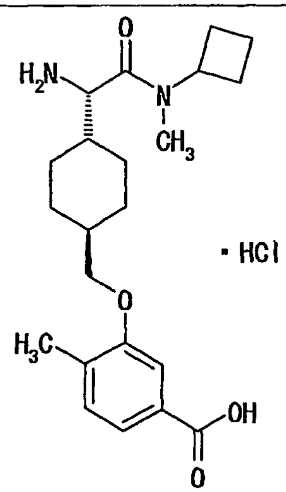
Example 358		^{1}H-NMR(δppm, DMSO-d_6) 0.95-1.30 (4H, m), 1.56-1.77 (6H, m), 1.81-2.34 (6H, m), 2.89 (1.74H, s), 2.99 (1.26H, s), 3.91 (2H, d, J=6.0Hz), 4.15 (0.42H, d, J=5.6Hz), 4.30 (0.58H, d, J=5.1Hz), 4.53-4.55 (0.58H, m), 4.76-4.79 (0.42H, m), 7.30-7.33 (1H, m), 7.54-7.59 (2H, m), 8.04 (3H, brs).
Example 359		^{1}H-NMR(δppm, DMSO-d_6) 1.01-1.29 (4H, m), 1.54-1.75 (6H, m), 1.85-2.37 (6H, m), 2.30 (3H, s), 2.89 (1.74H, s), 2.99 (1.26H, s), 3.80 (2H, d, J=6.0Hz), 4.14 (0.42H, d, J=5.6Hz), 4.29 (0.58H, d, J=5.6Hz), 4.47-4.62 (0.58H, m), 4.72-4.83 (0.42H, m), 7.07 (1H, d, J=7.9Hz), 7.19 (1H, t, J=7.9Hz), 7.28 (1H, d, J=7.4Hz), 8.05 (3H, brs).
Example 360		^{1}H-NMR(δppm, DMSO-d_6) 1.00-1.29 (4H, m), 1.56-1.77 (6H, m), 1.85-2.35 (6H, m), 2.20 (3H, s), 2.89 (1.74H, s), 2.99 (1.26H, s), 3.82 (2H, d, J=6.0Hz), 4.14 (0.42H, d, J=5.1Hz), 4.28 (0.58H, d, J=5.6Hz), 4.47-4.61 (0.58H, m), 4.72-4.84 (0.42H, m), 7.25 (1H, d, J=7.9Hz), 7.37 (1H, s), 7.43 (1H, d, J=7.9Hz), 7.99 (3H, brs).

Table 1-104

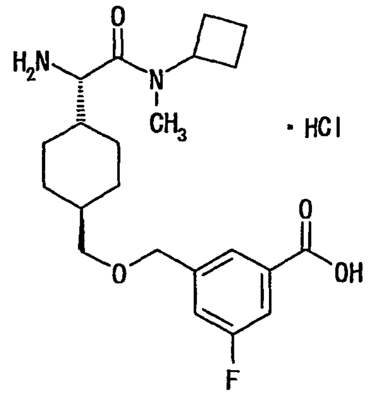
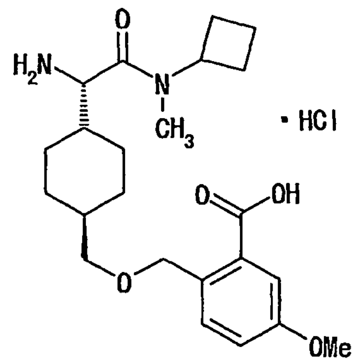
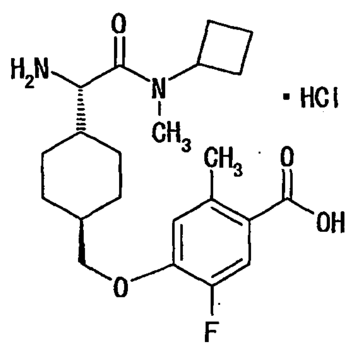
Example 361		^{1}H-NMR(δppm, DMSO-d_6) 0.80-1.27 (4H, m), 1.43-1.84 (8H, m), 1.94-2.35 (4H, m), 2.88 (1.74H, s), 2.97 (1.26H, s), 3.25 (2H, d, J=6.0Hz), 4.13 (0.42H, d, J=5.1Hz), 4.27 (0.58H, d, J=5.6Hz), 4.45-4.58 (0.58H, m), 4.51 (2H, s), 4.70-4.81 (0.42H, m), 7.38 (1H, d, J=8.3Hz), 7.55 (1H, d, J=8.3Hz), 7.72 (1H, s), 8.05 (3H, brs).
Example 362		^{1}H-NMR(δppm, DMSO-d_6) 0.79-1.28 (4H, m), 1.40-1.84 (8H, m), 1.94-2.34 (4H, m), 2.88 (1.74H, s), 2.97 (1.26H, s), 3.23 (2H, d, J=6.0Hz), 3.77 (3H, s), 4.13 (0.42H, d, J=5.6Hz), 4.28 (0.58H, d, J=5.6Hz), 4.47-4.57 (0.58H, m), 4.66 (2H, s), 4.72-4.84 (0.42H, m), 7.10 (1H, dd, J=8.3, 2.8Hz), 7.30 (1H, d, J=2.8Hz), 7.44 (1H, d, J=8.3Hz), 8.03 (3H, brs).
Example 363		^{1}H-NMR(δppm, DMSO-d_6) 0.97-1.25 (4H, m), 1.60-1.63 (6H, m), 1.86-1.89 (2H, m), 1.97-2.19 (3H, m), 2.28-2.30 (1H, m), 2.50 (3H, s), 2.88 (1.74H, s), 2.98 (1.26H, s), 3.91 (2H, d, J=6.5Hz), 4.14 (0.42H, d, J=5.1Hz), 4.29 (0.58H, d, J=5.1Hz), 4.52-4.54 (0.58H, m), 4.75-4.78 (0.42H, m), 7.06 (1H, d, J=8.3Hz), 7.59 (1H, d, J=12.5Hz), 8.05 (1H, brs).

Table 1-105

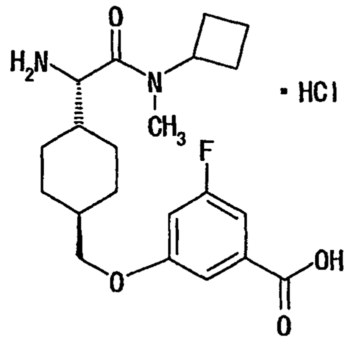
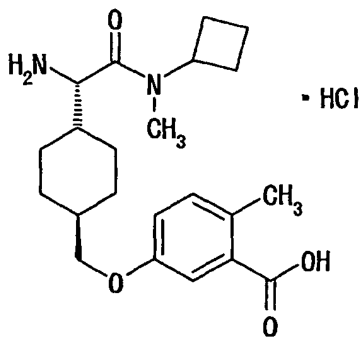
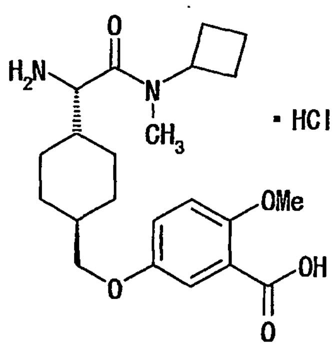
Example 364		^{1}H-NMR(δppm, DMSO-d_6) 0.91-1.33 (4H, m), 1.54-1.72 (6H, m), 1.80-1.91 (2H, m), 1.95-2.23 (3H, m), 2.21-2.36 (1H, m), 2.88 (1.74H, s), 2.98 (1.26H, s), 3.84 (2H, d, J=6.5Hz), 4.14 (0.42H, d, J=5.6Hz), 4.29 (0.58H, d, J=5.6Hz), 4.47-4.60 (0.58H, m), 4.69-4.81 (0.42H, m), 7.07 (1H, dt, J=10.7, 2.3Hz), 7.21 (1H, d, J=8.8Hz), 7.25 (1H, brs), 8.05 (3H, brs).
Example 365		^{1}H-NMR(δppm, DMSO-d_6) 0.93-1.28 (4H, m), 1.53-1.74 (6H, m), 1.80-1.91 (2H, m), 1.95-2.21 (3H, m), 2.21-2.34 (1H, m), 2.39 (3H, s), 2.88 (1.74H, s), 2.98 (1.26H, s), 3.76 (2H, d, J=6.0Hz), 4.14 (0.42H, d, J=5.1Hz), 4.29 (0.58H, d, J=5.1Hz), 4.46-4.60 (0.58H, m), 4.68-4.83 (0.42H, m), 6.99 (1H, dd, J=8.3, 2.8Hz), 7.17 (1H, d, J=8.3Hz), 7.29 (1H, d, J=2.8Hz), 8.07 (3H, brs).
Example 366		^{1}H-NMR(δppm, DMSO-d_6) 0.88-1.31 (4H, m), 1.53-1.74 (6H, m), 1.80-1.92 (2H, m), 1.94-2.19 (3H, m), 2.21-2.33 (1H, m), 2.88 (1.74H, s), 2.97 (1.26H, s), 3.73 (2H, d, J=8.2Hz), 3.74 (3H, s), 4.14 (0.42H, d, J=5.1Hz), 4.29 (0.58H, d, J=5.1Hz), 4.45-4.60 (0.58H, m), 4.66-4.84 (0.42H, m), 6.99-7.09 (2H, m), 7.12 (1H, d, J=2.8Hz), 8.08 (3H, brs).

Table 1-106

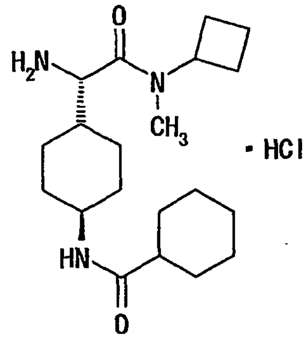
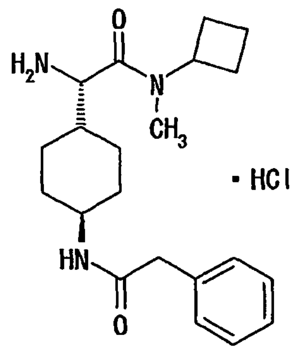
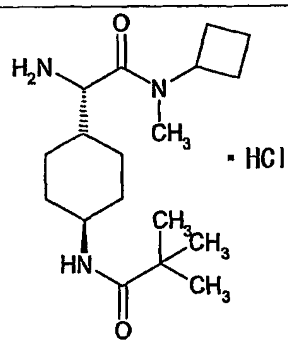
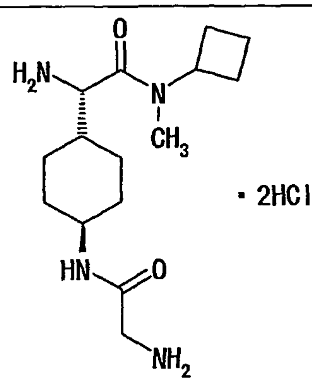
Example 367		^{1}H-NMR(δppm, DMSO-d_6) 0.93-1.43(9H, m), 1.47-1.85(12H, m), 1.93-2.40(5H, m), 2.89(1.7H, s), 2.98(1.3H, s), 3.27-3.51(1H, m), 4.08-4.21(0.4H, m), 4.21-4.39(0.6H, m), 4.44-4.62 (0.6H, m), 4.66-4.85(0.4H, m), 7.52(1H, d, J=7.9Hz), 8.10(3H, brs).
Example 368		^{1}H-NMR(δppm, DMSO-d_6) 0.98-1.35(4H, m), 1.48-1.88(7H, m), 1.93-2.39(4H, m), 2.89(1.7H, s), 2.98(1.3H, s), 3.29-3.50(3H, m), 4.08-4.21(0.4H, m), 4.22-4.37(0.6H, m), 4.44-4.63 (0.6H, m), 4.66-4.85(0.4H, m), 7.12-7.36(5H, m), 8.00(1H, d, J=7.9Hz), 8.10(3H, brs).
Example 369		^{1}H-NMR(δppm, DMSO-d_6) 1.06(9H, s), 1.10-1.32(4H, m), 1.48-1.83(7H, m), 1.94-2.39(4H, m), 2.89(1.8H, s), 2.99(1.2H, s), 3.28-3.60(1H, m), 4.08-4.22(0.4H, m), 4.22-4.38(0.6H, m), 4.47-4.64(0.6H, m), 4.68-4.85 (0.4H, m), 7.12(1H, d, J=8.3Hz), 8.11(3H, brs).
Example 370		^{1}H-NMR(δppm, DMSO-d_6) 0.99-1.38(4H, m), 1.49-1.89(7H, m), 1.92-2.40(4H, m), 2.89(1.8H, s), 2.99(1.2H, s), 3.36-3.59(3H, m), 4.08-4.19(0.4H, m), 4.22-4.34(0.6H, m), 4.42-4.64(0.6H, m), 4.65-4.85(0.4H, m), 8.15(5H, brs), 8.35-8.50(1H, m).

Table 1-107

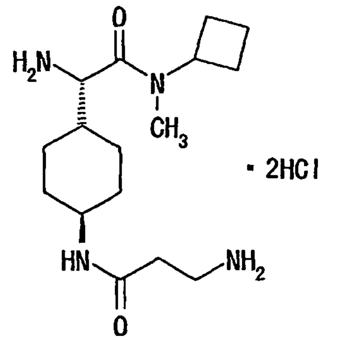
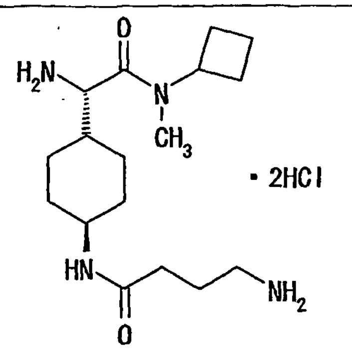
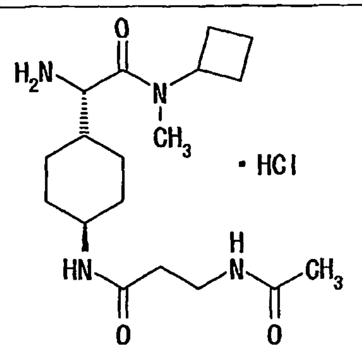
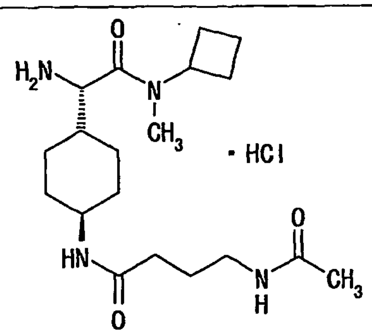
Example 371		^{1}H-NMR(δppm, DMSO-d_6) 1.00-1.34(4H, m), 1.48-1.88(7H, m), 1.93-2.37(4H, m), 2.45(2H, t, J=7.2Hz), 2.80-3.05 (5H, m), 3.25-3.54(1H, m), 4.06-4.20 (0.4H, m), 4.21-4.38(0.6H, m), 4.43-4.63(0.6H, m), 4.66-4.86 (0.4H, m), 7.80-8.29(7H, m).
Example 372		^{1}H-NMR(δppm, DMSO-d_6) 0.98-1.36(4H, m), 1.48-1.90(9H, m), 1.90-2.40(6H, m), 2.65-2.81(2H, m), 2.89(1.8H, s), 2.98(1.2H, s), 3.31-3.52(1H, m), 4.03-4.44(1H, m), 4.45-4.63(0.6H, m), 4.66-4.84(0.4H, m), 7.82-8.32 (7H, m).
Example 373		^{1}H-NMR(δppm, DMSO-d_6) 0.95-1.33(4H, m), 1.48-1.87(7H, m), 1.77(3H, s), 1.91-2.41(6H, m), 2.89(1.8H, s), 2.98(1.2H, s), 3.12-3.25(2H, m), 3.31-3.54(1H, m), 4.06-4.20(0.4H, m), 4.20-4.37(0.6H, m), 4.45-4.64(0.6H, m), 4.65-4.85(0.4H, m), 7.77(1H, d, J=8.3Hz), 7.87(1H, brs), 8.13(3H, brs).
Example 374		^{1}H-NMR(δppm, DMSO-d_6) 0.94-1.33(4H, m), 1.47-1.87(9H, m), 1.78(3H, s), 1.91-2.38(6H, m), 2.89(1.8H, s), 2.92-3.04(3.2H, m), 3.31-3.51(1H, m), 4.07-4.21(0.4H, m), 4.22-4.36 (0.6H, m), 4.44-4.63(0.6H, m), 4.67-4.84(0.4H, m), 7.66-7.80(1H, m), 7.87(1H, brs), 8.12(3H, brs).

Table 1-108

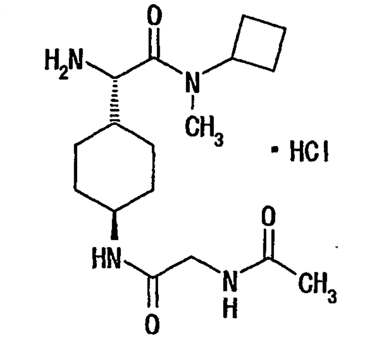
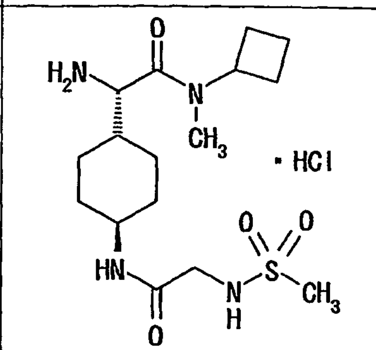
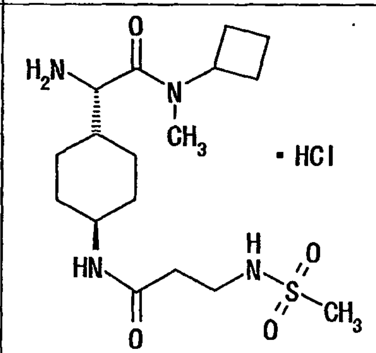
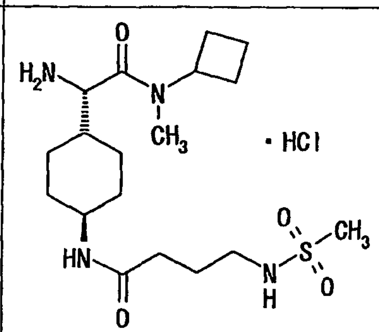
Example 375		^{1}H-NMR(δppm, DMSO-d_6) 0.99-1.36(4H, m), 1.45-1.88(7H, m), 1.83(3H, s), 1.89-2.39(4H, m), 2.89(1.8H, s), 2.98(1.2H, s), 3.34-3.52(1H, m), 3.55-3.65(2H, m), 4.08-4.21(0.4H, m), 4.22-4.35(0.6H, m), 4.44-4.61 (0.6H, m), 4.67-4.83(0.4H, m), 7.66-7.80(1H, m), 7.90-8.24(4H, m).
Example 376		^{1}H-NMR(δppm, DMSO-d_6) 1.01-1.37(4H, m), 1.49-1.88(7H, m), 1.92-2.39(4H, m), 2.89(1.8H, s), 2.91(3H, s), 2.98(1.2H, s), 3.31-3.45(1H, m), 4.08-4.20(0.4H, m), 4.22-4.37(0.6H, m), 4.46-4.61(0.6H, m), 4.68-4.83 (0.4H, m), 7.30(1H, t, J=6.0Hz), 7.77-7.89(1H, m), 8.10(3H, brs).
Example 377		^{1}H-NMR(δppm, DMSO-d_6) 0.96-1.35(4H, m), 1.49-1.88(7H, m), 1.92-2.38(6H, m), 2.87(3H, s), 2.89(1.8H, s), 2.98(1.2H, s), 3.06-3.17(2H, m), 3.34-3.51(1H, m), 4.08-4.20(0.4H, m), 4.23-4.35(0.6H, m), 4.45-4.62 (0.6H, m), 4.67-4.84(0.4H, m), 6.88-7.03(1H, m), 7.75-7.87(1H, m), 8.10(3H, brs).
Example 378		^{1}H-NMR(δppm, DMSO-d_6) 0.94-1.37(4H, m), 1.48-1.87(9H, m), 1.92-2.39(6H, m), 2.79-2.95(2H, m), 2.86(3H, s), 2.88(1.8H, s), 2.98(1.2H, s), 3.29-3.52(1H, m), 4.08-4.21(0.4H, m), 4.23-4.34(0.6H, m), 4.45-4.61(0.6H, m), 4.67-4.84(0.4H, m), 6.97(1H, brs), 7.65-7.78(1H, m), 8.10(3H, brs).

Table 1-109

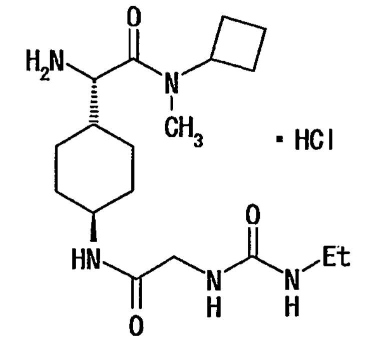
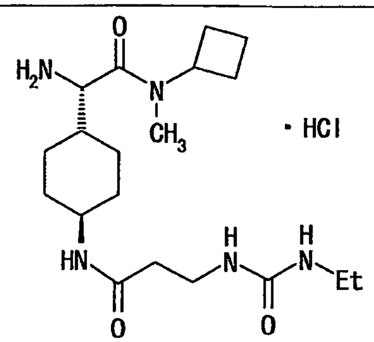
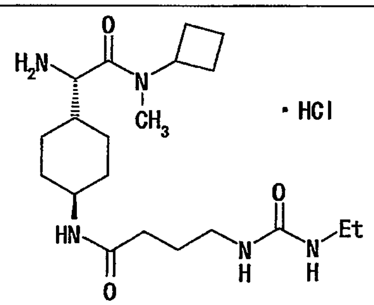
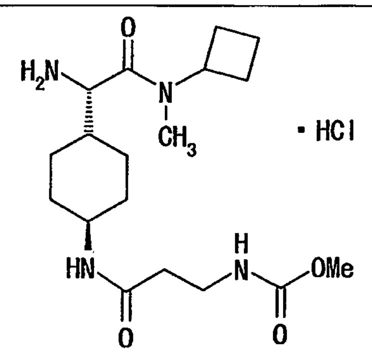
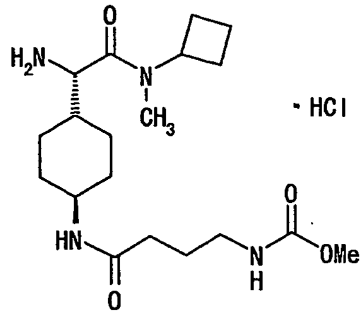
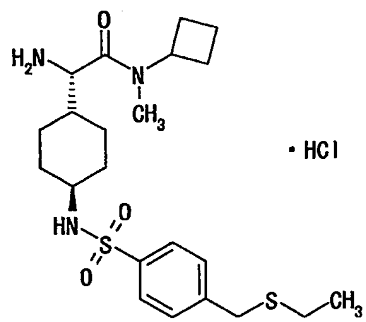
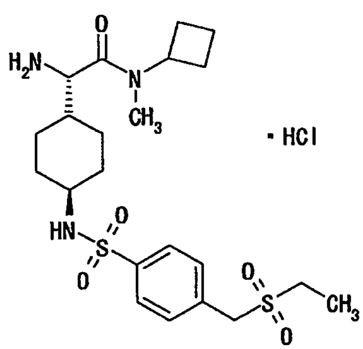
Example 379		^{1}H-NMR(δppm, DMSO-d_6) 0.97(3H, t, J=7.2Hz), 1.02-1.35(4H, m), 1.50-1.86 (7H, m), 1.92-2.37(4H, m), 2.89(1.8H, s), 2.98(1.2H, s), 2.99(2H, q, J=7.2Hz), 3.35-3.50(1H, m), 3.55(2H, s), 4.07-4.19(0.4H, m), 4.23-4.35 (0.6H, m), 4.45-4.61(0.6H, m), 4.67-4.83(0.4H, m), 7.64-7.73(1H, m), 8.10(3H, brs).
Example 380		^{1}H-NMR(δppm, DMSO-d_6) 0.96(3H, t, J=7.2Hz), 1.00-1.34(4H, m), 1.49-1.87 (7H, m), 1.92-2.38(6H, m), 2.88(1.8H, s), 2.97(2H, q, J=7.2Hz), 2.98(1.2H, s), 3.09-3.21(2H, m), 3.34-3.51(1H, m), 4.07-4.19(0.4H, m), 4.21-4.36 (0.6H, m), 4.45-4.61(0.6H, m), 4.67-4.83(0.4H, m), 7.69-7.82(1H, m), 8.11(3H, brs).
Example 381		^{1}H-NMR(δppm, DMSO-d_6) 0.96(3H, t, J=7.0Hz), 1.01-1.34(4H, m), 1.46-1.87 (9H, m), 1.92-2.38(6H, m), 2.83-3.05 (7H, m), 3.33-3.50(1H, m), 4.07-4.20 (0.4H, m), 4.22-4.35(0.6H, m), 4.46-4.61(0.6H, m), 4.68-4.83(0.4H, m), 7.70-7.82(1H, m), 8.12(3H, brs).
Example 382		^{1}H-NMR(δppm, DMSO-d_6) 0.94-1.35(4H, m), 1.49-1.72(5H, m), 1.72-1.86(2H, m), 1.92-2.38(6H, m), 2.88(1.8H, s), 2.98(1.2H, s), 3.07-3.21(2H, m), 3.32-3.61(1H, m), 3.50(3H, s), 4.08-4.18(0.4H, m), 4.24-4.34(0.6H, m), 4.46-4.61(0.6H, m), 4.68-4.83(0.4H, m), 7.06(1H, brs), 7.68-7.83(1H, m), 8.10(3H, brs).

Table 1-110

Example 383		^{1}H-NMR(δppm, DMSO-d_6) 0.94-1.35(4H, m), 1.49-1.72(7H, m), 1.72-1.86(2H, m), 1.91-2.37(6H, m), 2.81-3.03(2H, m), 2.88(1.8H, s), 2.98(1.2H, s), 3.32-3.59(1H, m), 3.50(3H, s), 4.06-4.19(0.4H, m), 4.22-4.36(0.6H, m), 4.46-4.61(0.6H, m), 4.67-4.82 (0.4H, m), 7.10(1H, brs), 7.63-7.76 (1H, m), 8.13(3H, brs).
Example 384		^{1}H-NMR(δppm, DMSO-d_6) 0.94-1.22(4H, m), 1.13(3H, t, J=7.5Hz), 1.36-1.74 (7H, m), 1.88-2.33(4H, m), 2.39(2H, q, J=7.5Hz), 2.69-2.90(1H, m), 2.85 (1.8H, s), 2.93(1.2H, s), 3.82(2H, s), 4.00-4.11(0.4H, m), 4.14-4.26(0.6H, m), 4.36-4.56(0.6H, m), 4.62-4.83 (0.4H, m), 7.52(2H, d, J=8.3Hz), 7.60-7.70(1H, m), 7.74(2H, d, J=8.3Hz),8.00(3H, brs).
Example 385		^{1}H-NMR(δppm, DMSO-d_6) 0.95-1.18(4H, m), 1.21(3H, t, J=7.5Hz), 1.41-1.74 (7H, m), 1.89-2.32(4H, m), 2.75-2.90 (1H, m), 2.85(1.8H, s), 2.93(1.2H, s), 3.07(2H, q, J=7.5Hz), 3.99-4.12(0.4H, m), 4.14-4.28(0.6H, m), 4.38-4.54 (0.6H, m), 4.60(2H, s), 4.64-4.80 (0.4H, m), 7.60(2H, d, J=8.3Hz), 7.71-7.80(1H, m),7.83(2H, d, J=8.3Hz), 8.03(3H, brs).

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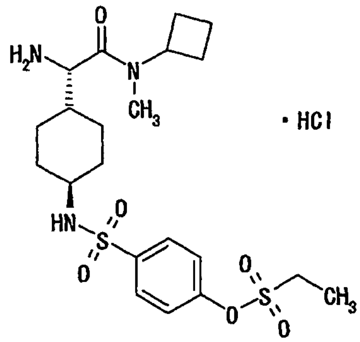
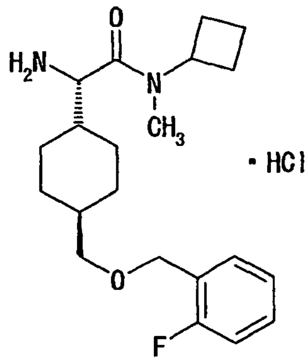
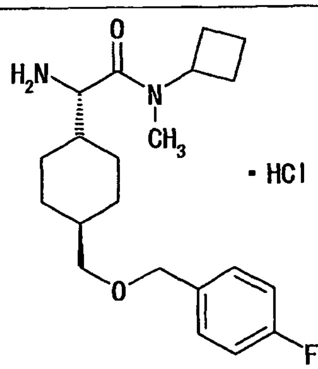
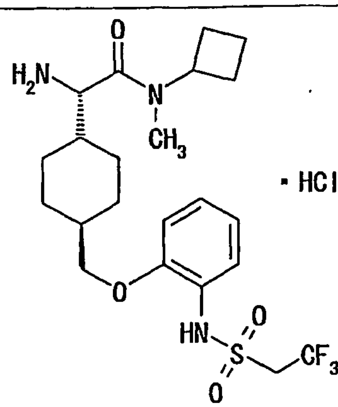
Example 386		^{1}H-NMR(δppm, DMSO-d_6) 0.93-1.26(4H, m), 1.39(3H, t, J=7.5Hz), 1.44-1.76 (7H, m), 2.76-2.91(1H, m), 2.86(1.8H, s), 2.93(1.2H, s), 3.62(2H, q, J=7.5Hz), 4.01-4.12(0.4H, m), 4.17-4.26(0.6H, m), 4.37-4.56 (0.6H, m), 4.63-4.81(0.4H, m), 7.54(2H, d, J=8.7Hz), 7.77-7.89 (1H, m), 7.90(2H, d, J=8.7Hz), 8.02(3H, brs).
Example 387		^{1}H-NMR(δppm, DMSO-d_6) 0.75-1.01(2H, m), 1.01-1.27(2H, m), 1.35-1.85(8H, m), 1.92-2.36(4H, m), 2.88(1.8H, s), 2.97(1.2H, s), 3.24(2H, d, J=6.0Hz), 4.07-4.18(0.4H, m), 4.23-4.33(0.6H, m), 4.43-4.60 (0.6H, m), 4.48(2H, s), 4.68-4.84 (0.4H, m), 7.11-7.25(2H, m), 7.29-7.48(2H, m), 8.06(3H, brs).
Example 388		^{1}H-NMR(δppm, DMSO-d_6) 0.78-1.00(2H, m), 1.00-1.29(2H, m), 1.35-1.84(8H, m), 1.92-2.36 (4H, m), 2.88(1.8H, s), 2.97 (1.2H, s), 3.21(2H, d, J=6.2Hz), 4.09-4.17(0.4H, m), 4.24-4.32 (0.6H, m), 4.40(2H, s), 4.46-4.60 (0.6H, m), 4.68-4.83(0.4H, m), 7.10-7.21(2H, m), 7.27-7.39(2H, m), 8.06(3H, brs).
Example 389		^{1}H-NMR(δppm, DMSO-d_6) 0.86-1.33(4H, m), 1.50-1.82(6H, m), 1.85-2.40(6H, m), 2.90(1.8H, s), 3.00(1.2H, s), 3.81(2H, d, J=6.4Hz), 4.10-4.24(0.4H, m), 4.26-4.47(2.6H, m), 4.47-4.67 (0.6H, m), 4.67-4.90(0.4H, m), 6.92(1H, dd, J=7.5Hz, 7.9Hz), 7.04(1H, d, J=7.9Hz), 7.15-7.34 (2H, m), 8.21(3H, brs).

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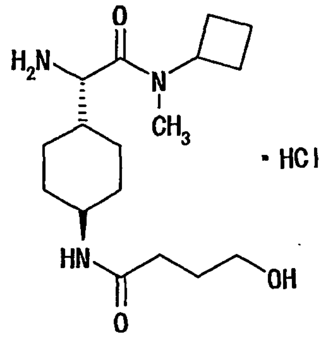
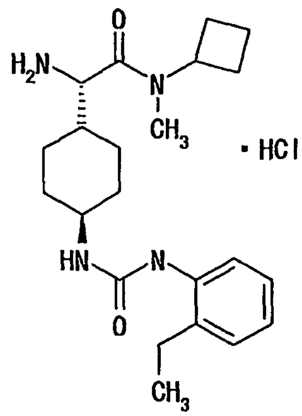
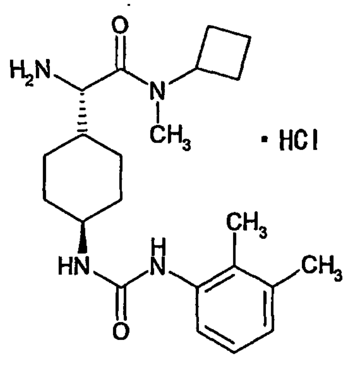
Example 390		^{1}H-NMR(δppm, DMSO-d_6) 8.04 (3H, s), 7.76 (1H, s), 4.85-4.70(0.47H, m),4.60-4.50(0.53H, m), 4.35-4.25 (0.47H, m),4.20-4.10(0.53H, m), 2.98 (1.2H, s), 2.89 (1.8H, s), 2.61 (1H, s), 2.31 (1H, m), 2.19-1.75 (8H, m), 1.70- 1.53 (6H, m), 1.31-1.00 (7H, m).
Example 391		^{1}H-NMR(δppm, DMSO-d_6) 8.06 (3H, s), 7.77 (1H, d, J=8.3Hz), 7.57 (1H, d, J=3.7Hz), 7.11-7.04 (2H, m), 6.91-6.87 (1H, m), 6.58 (1H, d, J=7.0Hz), 4.85-4.72 (0.42H, s), 4.59-4.50 (0.59H, m), 4.35-4.27 (0.59H, m), 4.20-4.15 (0.41H, m), 3.00 (1.3H, s), 2.90 (1.7H, s), 2.53 (2H, q, J=7.4Hz), 2.33-1.91 (7H, m), 1.75-1.57 (5H, m), 1.33-1.04 (7H, m).
Example 392		^{1}H-NMR(δppm, DMSO-d_6) 8.05 (3H, s), 7.60 (1H, s), 7.51 (1H, d, J=7.9Hz), 6.94 (1H, t, J=7.7Hz), 6.79 (1H, d, J=7.9Hz), 6.45 (1H, s), 4.83-4.72 (0.4H, m), 4.57-4.48 (0.6H, m), 4.35-4.25 (0.6H, m), 4.20-4.17 (0.4H, m), 3.37-3.29 (2H, m), 2.99 (1.3H, s), 2.90 (1.7H, s), 2.31 (1H, t, J=9.3Hz), 2.21 (3H, s), 2.19-2.13 (1H, m), 2.10-1.97 (5H, m), 1.95-1.88 (3H, m), 1.70-1.55 (5H, m), 1.29-1.18 (3H, m).

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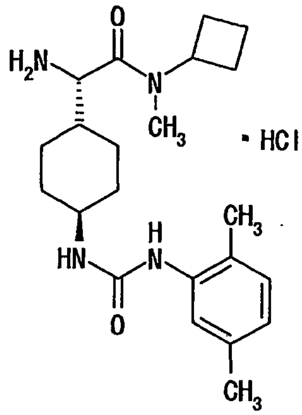
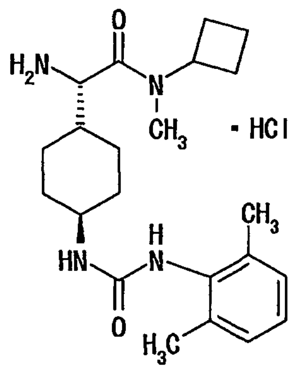
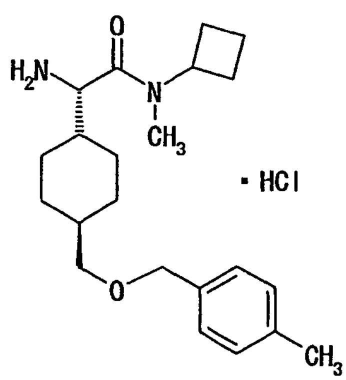
Example 393		^{1}H-NMR (δppm, DMSO-d_6) 8.07 (3H, s), 7.65 (1H, s), 7.55 (1H, d, J=3.7Hz), 6.95 (1H, d, J=7.9Hz), 6.65 (1H, d, J=7.4Hz), 6.60 (1H, d, J=6.5Hz), 4.82-4.75 (0.4H, m), 4.60-4.50 (0.6H, m), 4.35-4.29 (0.6H, m), 4.20-4.15 (0.4H, m), 3.37-3.25 (2H, m), 3.00 (1.3H, s), 2.90 (1.7H, s), 2.33-2.24 (1H, m), 2.20 (3H, s), 2.14 (1H, t, J=7.2Hz), 2.11 (3H, s), 2.10-1.88 (4H, m), 1.70-1.55 (5H,m), 1.30-1.05 (4H, m).
Example 394		^{1}H-NMR (δppm, DMSO-d_6) 8.06 (3H, brs), 7.43 (1H, s), 7.02-6.96 (3H, m), 5.99 (1H, s), 4.82-4.71 (0.4H,m), 4.64-4.46 (0.6H, m), 4.31 (0.6H, brs), 4.16 (0.4H, brs), 3.30 (1H, brs), 2.99 (1.3H, s), 2.89 (1.7H, s), 2.32-2.16 (1H, m), 2.12 (6H, s), 2.10-1.97 (3H,m), 1.95-1.85 (2H, m), 1.70-1.53 (5H, m), 1.30-1.06 (4H, m).
Example 395		^{1}H-NMR (δppm, DMSO-d_6) 8.04 (2H, brs), 7.18 (2H, d, J=7.7Hz), 7.14 (2H, d, J=7.7Hz), 4.77 (0.4H, t, J=8.8Hz), 4.53 (0.6H, t, J=8.1Hz), 4.39 (2H, s), 4.29 (0.6H, d, J=4.6Hz), 4.14 (0.4H, d, J=5.1Hz), 3.18 (2H, dd, J=9.7, 5.6Hz), 2.98 (1.3H, s), 2.89 (1.7H, s), 2.30 (4H, brs), 2.20-2.01 (3H, m), 1.77 (2H, brs), 1.73-1.50 (5H,m), 1.49-1.41 (1H, m), 1.29-1.10 (3H, m), 0.95-0.85 (2H, m).

Table 1-114

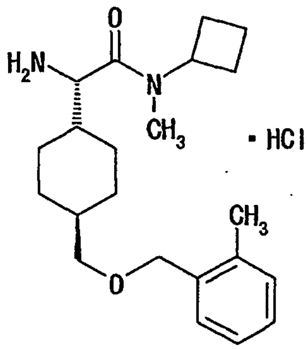
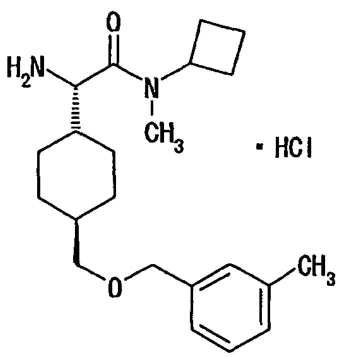
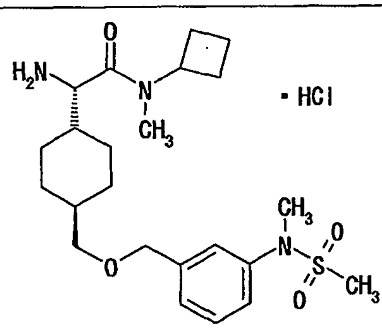
Example 396		^{1}H-NMR(δppm, DMSO-d_6) 8.06 (2H, brs), 7.26 (1H, d, J=6.5Hz), 7.18-7.13 (3H, m), 4.77 (0.4H, t, J=9.3Hz), 4.53 (0.6H, t, J=8.1Hz), 4.43 (2H, s), 4.30 (0.4H, brs), 4.13 (0.6H, brs), 3.24 (1.5H, d, J=6.0Hz), 3.17 (0.5H, d, J=4.6Hz), 2.98 (1.3H, s), 2.89 (1.7H, s), 2.30-2.23 (5H, m), 2.20-1.95 (3H, m), 1.83-1.72 (2H, m), 1.70-1.55 (6H, m), 1.53-1.40 (1H, m), 1.22-1.10 (2H, m), 0.98-0.85 (1H, m).
Example 397		^{1}H-NMR(δppm, DMSO-d_6) 8.01 (2H, brs), 7.22 (1H, t, J=7.2Hz), 7.12-7.06 (3H,m), 4.77 (0.4H, t, J=8.1Hz), 4.53 (0.6H, t, J=8.1Hz), 4.39 (2H, s), 4.31-4.27 (0.6H, m), 4.16-4.12 (0.4H, m), 3.21 (2H, d, J=6.5Hz), 2.98 (1.3H, s), 2.89 (1.7H, s), 2.30 (3H, s), 2.25-2.00 (4H, m), 1.85-1.75 (2H, m), 1.70-1.52 (5H, m), 1.50-1.40 (1H, m), 1.25-0.80 (5H, m).
Example 398		^{1}H-NMR(δppm, DMSO-d_6) 8.00(3H, brs), 7.41-7.22(4H, m), 4.82-4.77(0.4H, m), 4.60-4.55(0.6H, m), 4.45 (2H, s), 4.37-4.30(0.6H, m), 4.21-4.15(0.4H, m), 3.22(3H, s), 2.98(1.2H, s), 2.93(3H, s), 2.89(1.8H, s), 2.38-2.00(4H, m), 1.85-1.75(2H, m), 1.73-1.45(6H, m), 1.08-0.85(3H, m).

Table 1-115

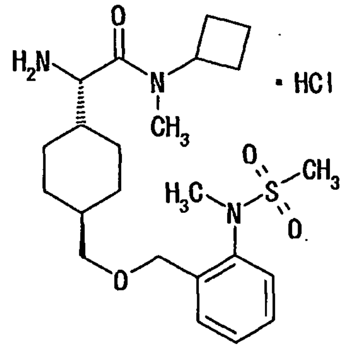
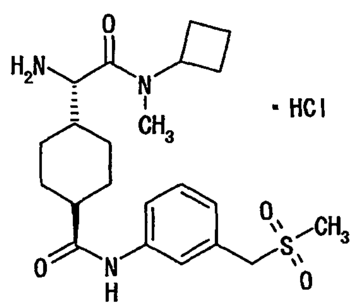
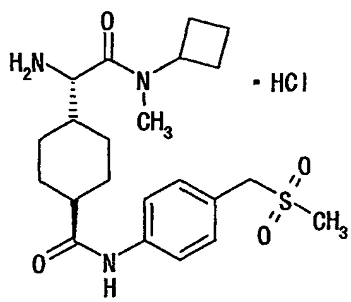
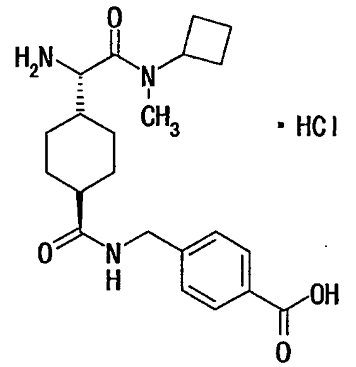
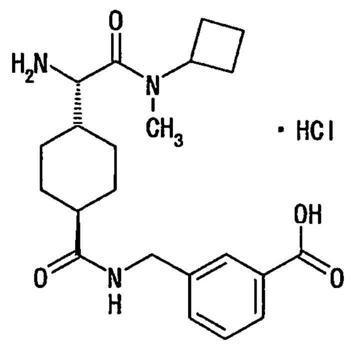
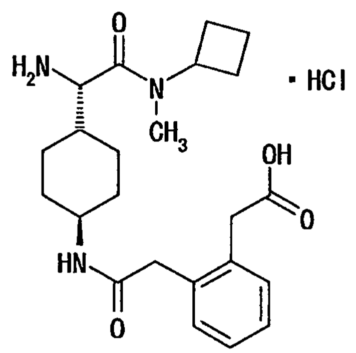
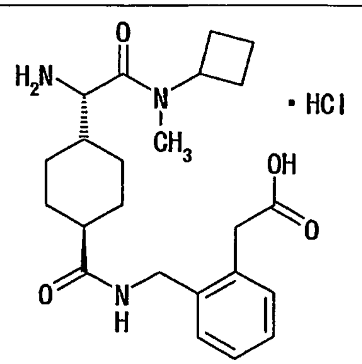
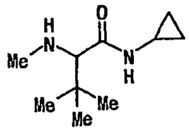
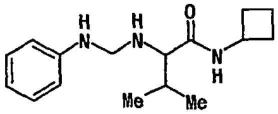
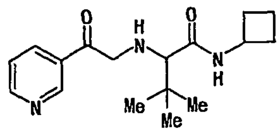
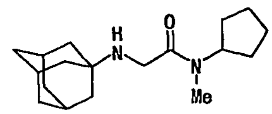
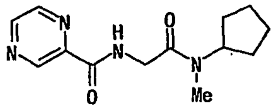
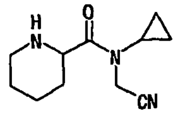
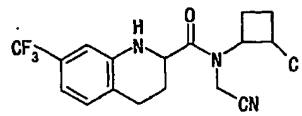
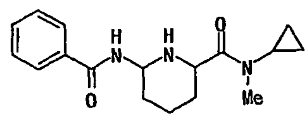
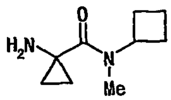
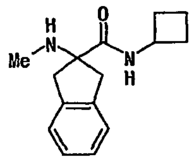
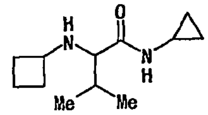
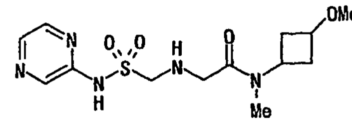
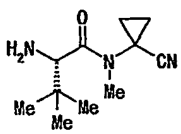
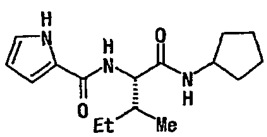
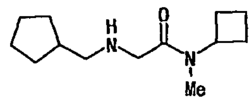
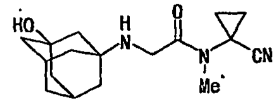
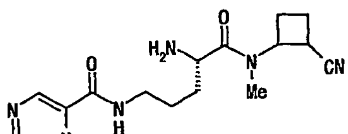
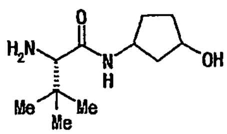
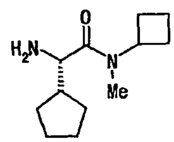
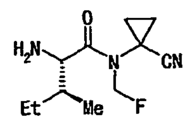
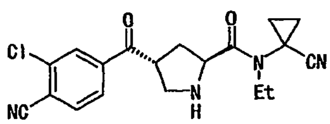
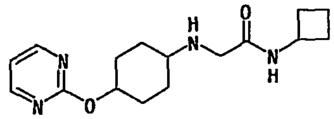
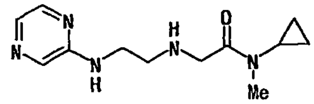
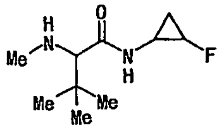
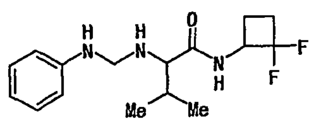
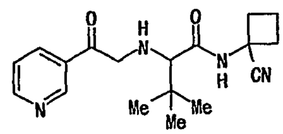
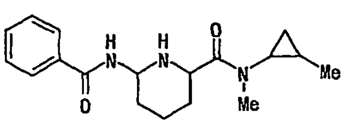
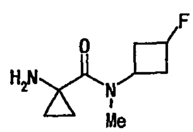
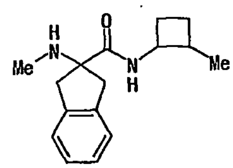
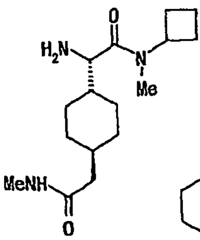
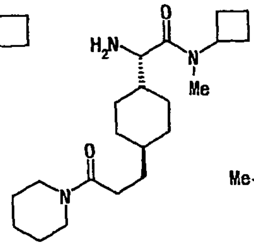
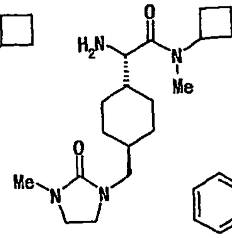
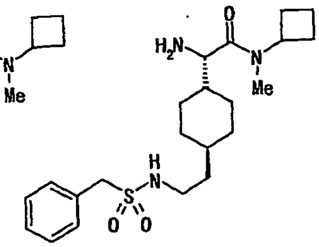
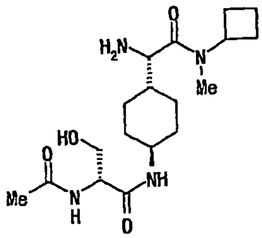
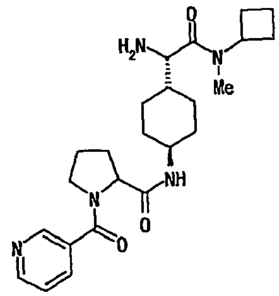
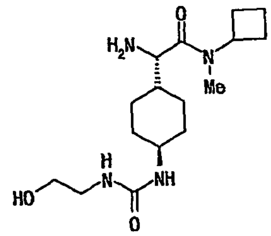
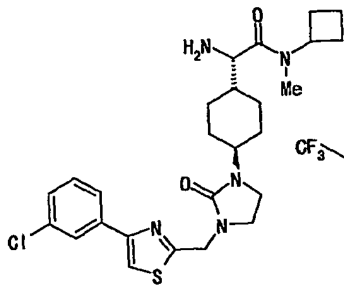
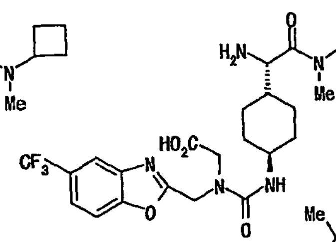
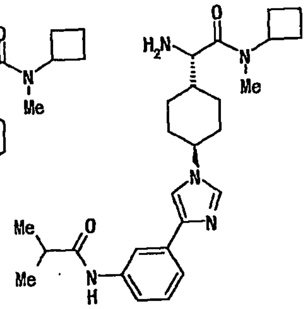
Example 399		^{1}H-NMR(δppm, DMSO-d_6) 8.00 (2H, brs), 7.50-7.45 (2H, m), 7.40-7.35 (2H, m), 4.82-4.70 (0.3H, m), 4.60-4.45 (0.7H, m), 4.35-4.25 (0.7H, m), 4.20-4.10 (0.3H,m), 3.25 (2H, d, J=6.0Hz), 3.13 (3H, s), 3.04 (3H, s), 2.97 (1.2H, s), 2.88 (1.8H, s), 2.30-2.00 (3H, m), 1.85- 1.77 (2H, m), 1.70-1.40 (6H, m), 1.25-0.80 (3H, m).
Example 400		^{1}H-NMR(δppm, DMSO-d_6) 8.39 (1H, t, J=5.8Hz), 8.09 (3H, brs), 7.87 (2H, d, J=8.3Hz), 7.32 (2H, d, J=8.3Hz), 4.76 (0.4H, t, J=8.8Hz), 4.54 (0.5H, t, J=8.6Hz), 4.45-4.27 (3.6H, m), 4.20-4.15 (0.4H, m), 2.98 (1.4H, s), 2.89 (1.6H, s), 2.28-2.02 (5H, m), 1.85-1.77 (3H, m), 1.70-1.55 (6H, m), 1.42-1.23 (3H, m).
Example 401		^{1}H-NMR(δppm, DMSO-d_6) 9.99 (1H, s), 8.10 (3H, brs), 7.60 (2H, d, J=8.3Hz), 7.30 (2H, d, J=8.8Hz), 4.77 (0.5H, t, J=8.3Hz), 4.56 (0.5H, t, J=8.1Hz), 4.38 (3H, s), 4.30-4.15 (1H, m), 3.00 (1.2H, s), 2.90 (1.8H, s), 2.85 (3H, s), 2.83-2.80 (1H,m), 2.33-2.06 (4H, m), 1.91-1.40 (3H, m), 1.75-1.60 (5H, m), 1.43-1.21 (2H, m).

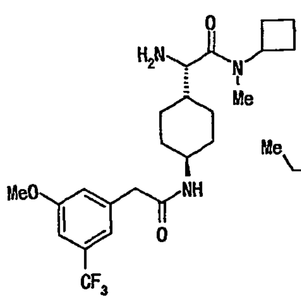
Table 1-116

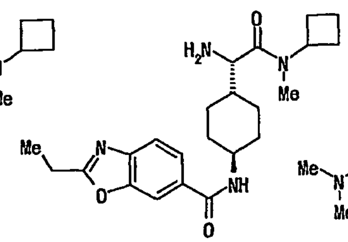
Example 402		^{1}H-NMR(δppm, DMSO-d_6) 8.39 (1H, t, J=5.8Hz), 8.09 (3H, brs), 7.87 (2H, d, J=8.3Hz), 7.32 (2H, d, J=8.3Hz), 4.76 (0.4H, t, J=8.6Hz), 4.54 (0.6H, t, J=8.6Hz), 4.31-4.27 (2.4H, m), 4.17 (0.6H, brs), 2.98 (1.2H, s), 2.89 (1.8H, s), 2.29-2.00 (6H, m), 1.85-1.75 (3H, m), 1.70-1.58 (6H, m), 1.41-1.20 (3H, m).
Example 403		^{1}H-NMR(δppm, DMSO-d_6) 8.35 (1H, s), 8.05 (3H, brs), 7.77 (2H, t, J=2.8Hz), 7.41 (2H, dt, J=13.0, 5.2Hz), 4.74 (0.4H, t, J=8.6Hz), 4.52 (0.6H, t, J=8.6Hz), 4.29 (0.6H, brs), 4.26 (2H, d, J=6.0Hz), 4.15 (0.4H, brs), 2.96 (1.4H, s), 2.87 (1.6H, s), 2.30-2.00 (6H, m), 1.80-1.73 (3H, m), 1.62-1.53 (6H, m), 1.40-1.20 (3H, m).
Example 404		^{1}H-NMR(δppm, DMSO-d_6) 8.04 (3H, brs), 7.95(1H, d, J=7.0Hz), 7.19-7.13(4H, m), 4.73 (0.4H, t, J=8.8Hz), 4.50 (0.6H, t, J= 8.1Hz), 4.27(0.6H, brs), 4.13(0.4H, brs), 3.63(2H, s), 3.38(2H, brs), 2.95(1.2H, s), 2.86(1.8H, s), 2.30-2.00(4H, m), 1.85-1.75(3H, m), 1.70-1.55(5H, m), 1.25-1.05(4H, m).
Example 405		^{1}H-NMR(δppm, DMSO-d_6) 8.13(1H, t, J=5.8Hz), 8.02(3H, brs), 7.22-7.13 (4H, m), 4.74 (0.5H, t, J=7.7Hz), 4.52(0.5H, t, J=7.7Hz), 4.30(0.5H, brs), 4.20(2H, d, J=5.6Hz), 4.16 (0.5H, brs), 3.61 (2H, s), 2.96 (1.3H, s), 2.87 (1.7H, s), 2.26-1.92 (6H, m), 1.85-1.70 (3H, m), 1.65-1.50 (5H, m), 1.36-1.05 (5H, m).

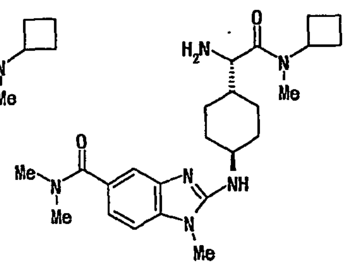
The present invention also comprises, but is not limited to, the following compounds.

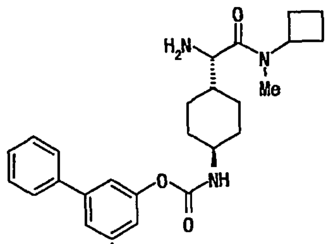






























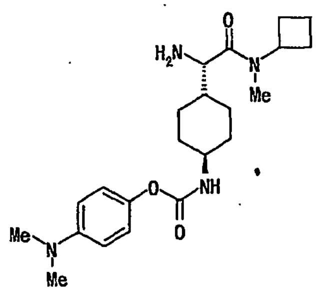











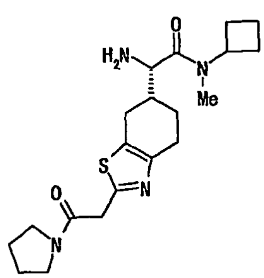


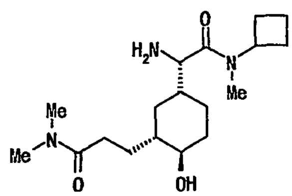


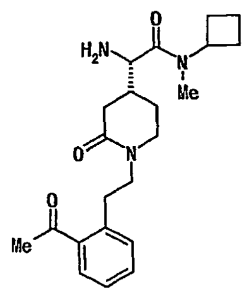


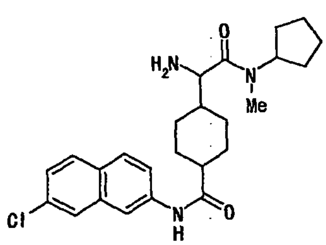
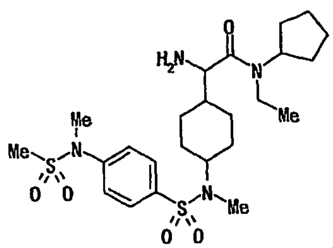
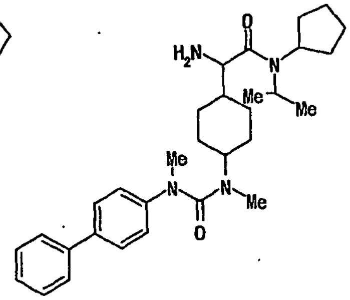
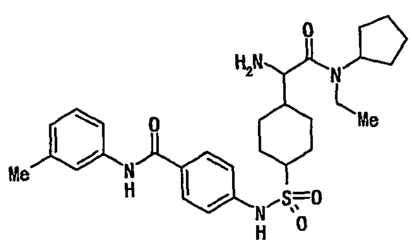
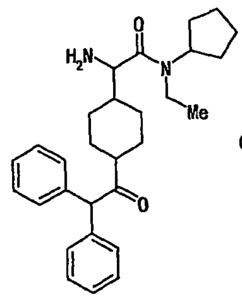
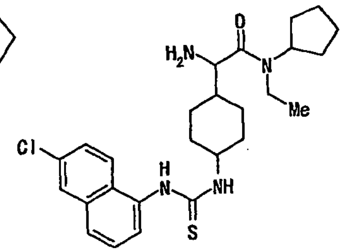
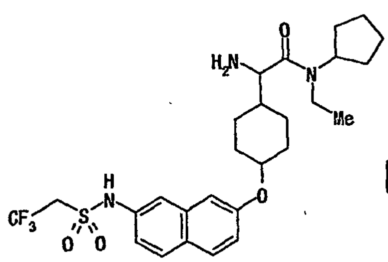
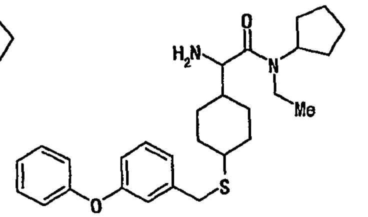
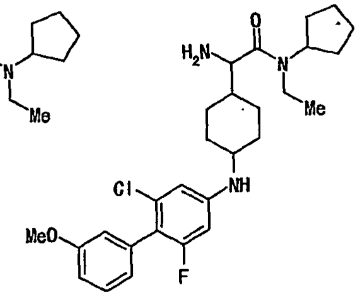


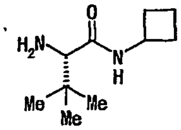
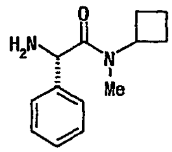
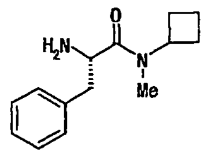
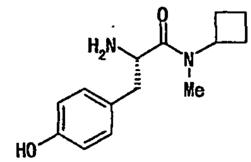


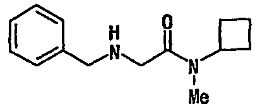
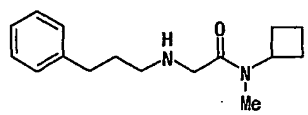
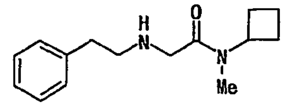


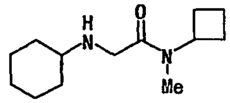
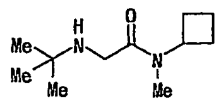
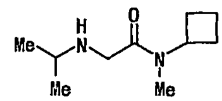


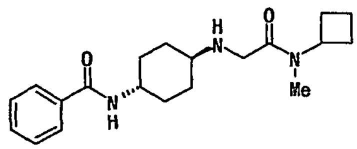
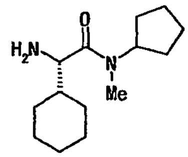
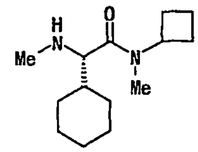


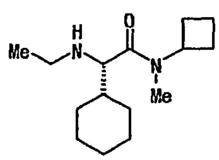
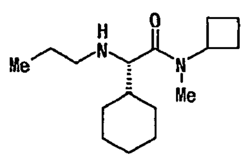
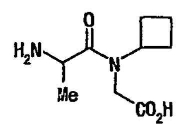
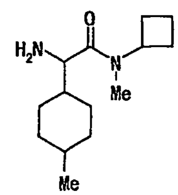










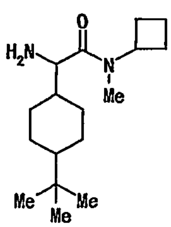
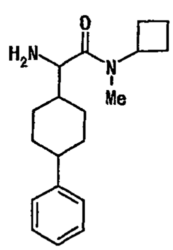
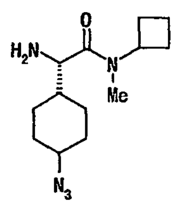
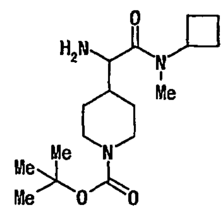
   

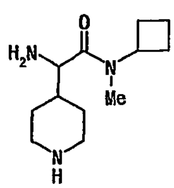
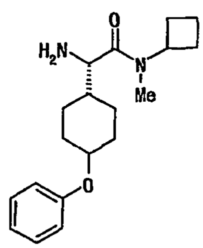
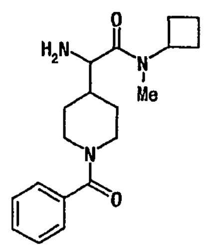
  

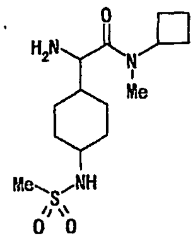
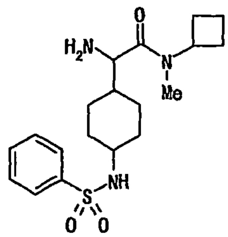
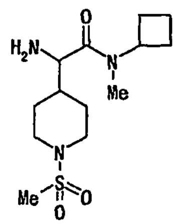
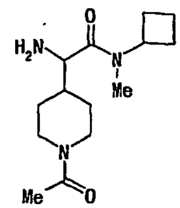
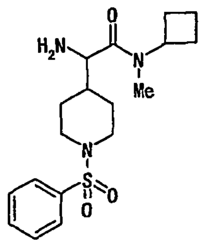
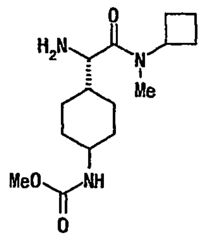
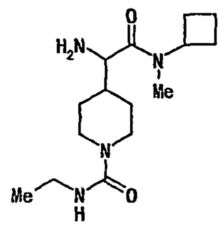
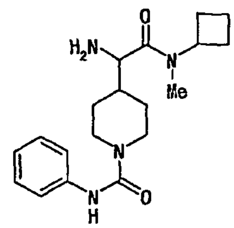
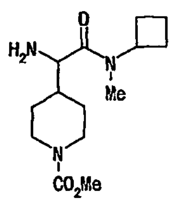
  

[Experimental Example]

Then, the biological activity of the compound of the present invention was examined.

Experimental Example 1: evaluation of human DPP-IV enzyme inhibitory activity

A test compound (10 μL/well) and D'PBS (70 μL/well, Dulbecco's Phosphate Buffered Saline, calcium, magnesium free, Sanko Junyaku Co., Ltd.) were added to a 96-well plate (FALCON) and stirred. Thereto was added 5 mM of synthetic substrate, Gly-Pro-pNA (Glycine-Proline-p-nitroaniline, PEPTIDE INSTITUTE, Inc.) at 10 μL/well and the mixture was stirred. Human DPP-IV purified enzyme was added at 10 μL/well, and after sufficient stirring, incubated at 37°C for 90 min.

The test compound was dissolved in dimethyl sulfoxide (Nacalai Tesque, Inc.) and the final concentration of dimethyl sulfoxide in reaction mixture was 0.1%.

After the completion of the reaction, the absorbance at (O.D.

405 nm)-(O.D. 650 nm) was measured using a microplate reader (Versa Max, Molecular Devices). The p-nitroaniline amount produced by DPP-IV enzyme was calculated from the standard curve of p-nitroaniline amount (Wako Pure Chemical Industries, Ltd.).

Using the following formula, an enzyme inhibition rate (%) was calculated and IC_{50} value was determined.

Enzyme inhibition rate (%) =

$$\left(1-\frac{\begin{pmatrix}\text{p-nitroaniline amount}\\ \text{of test compound}\end{pmatrix}-\begin{pmatrix}\text{p-nitroaniline}\\ \text{amount of blank}\end{pmatrix}}{\begin{pmatrix}\text{total amount of}\\ \text{p-nitroaniline}\end{pmatrix}-\begin{pmatrix}\text{p-nitroaniline}\\ \text{amount of blank}\end{pmatrix}}\right)\times 100$$

wherein the p-nitroaniline amount of blank shows the amount of p-nitroaniline of well free of enzyme, the total amount of p-nitroaniline shows the amount of p-nitroaniline of well free of the compound.

The results are shown in Tables 2-1 and 2-13.

Table 2-1

Test compound	IC_{50} (μM)
Example 1	< 10
Example 2	< 100
Example 4	< 100
Example 5	< 10
Example 6	< 10
Example 7	< 100
Example 8	< 10
Example 10	< 100
Example 14	< 10
Example 15	< 10
Example 19	< 10
Example 21	< 10
Example 22	< 10
Example 23	< 10
Example 26	< 100
Example 28	< 10
Example 29	< 10
Example 30	< 10
Example 31	< 10
Example 32	< 10
Example 33	< 10
Example 34	< 10
Example 35	< 10
Example 36	< 10
Example 37	< 10
Example 38	< 10
Example 39	< 10
Example 40	< 10
Example 41	< 10
Example 42	< 10
Example 43	< 10
Example 44	< 10
Example 45	< 10
Example 46	< 10
Example 47	< 10
Example 48	< 10
Example 49	< 10

Table 2-2

Test compound	IC_{50} (μM)
Example 50	< 10
Example 51	< 10
Example 52	< 10
Example 53	< 10
Example 54	< 10
Example 55	< 10
Example 56	< 10
Example 57	< 10

Table 2-3

Test compound	IC_{50} (μM)
Example 58	< 10
Example 59	< 10
Example 60	< 10
Example 61	< 10
Example 62	< 10
Example 63	< 10
Example 64	< 10
Example 65	< 10
Example 66	< 10
Example 67	< 10
Example 68	< 10
Example 69	< 10
Example 70	< 10
Example 71	< 10
Example 72	< 10
Example 73	< 10
Example 74	< 10
Example 75	< 10
Example 76	< 10
Example 77	< 10
Example 78	< 10
Example 79	< 10
Example 80	< 10

Table 2-4

Test compound	IC_{50} (μM)
Example 81	< 10
Example 82	< 10
Example 83	< 10
Example 84	< 10
Example 85	< 10
Example 86	< 10
Example 87	< 10
Example 88	< 10
Example 89	< 10
Example 90	< 10
Example 91	< 10
Example 92	< 10
Example 93	< 10
Example 94	< 10
Example 95	< 10
Example 96	< 10
Example 97	< 10
Example 98	< 10
Example 99	< 10
Example 100	< 10
Example 101	< 10
Example 102	< 10
Example 103	< 10
Example 104	< 10
Example 105	< 10
Example 106	< 10
Example 107	< 10
Example 108	< 10
Example 109	< 10
Example 110	< 10
Example 111	< 10
Example 112	< 10
Example 113	< 10

Table 2-5

Test compound	IC_{50} (μM)
Example 114	< 10
Example 115	< 10
Example 116	< 10
Example 117	< 10
Example 118	< 10
Example 119	< 10
Example 120	< 10
Example 121	< 10
Example 122	< 10
Example 123	< 10
Example 124	< 10
Example 125	< 10
Example 126	< 10
Example 127	< 10
Example 128	< 10
Example 129	< 10
Example 130	< 10
Example 131	< 10
Example 132	< 10
Example 133	< 10
Example 134	< 10
Example 135	< 10
Example 136	< 10
Example 137	< 10
Example 138	< 10
Example 139	< 10
Example 140	< 10
Example 141	< 10
Example 142	< 10
Example 143	< 10
Example 144	< 10
Example 145	< 10
Example 146	< 10

Table 2-6

Test compound	IC_{50} (μM)
Example 147	< 10
Example 148	< 10
Example 149	< 10
Example 150	< 10
Example 151	< 10
Example 152	< 10
Example 153	< 10
Example 154	< 10
Example 155	< 10
Example 156	< 10
Example 157	< 10
Example 158	< 10
Example 159	< 10
Example 160	< 10
Example 161	< 10
Example 162	< 10
Example 163	< 10
Example 164	< 10
Example 165	< 10
Example 166	< 10
Example 167	< 10
Example 168	< 10
Example 169	< 10
Example 170	< 10
Example 171	< 10
Example 172	< 10
Example 173	< 10
Example 174	< 10
Example 175	< 10
Example 176	< 10
Example 177	< 10
Example 178	< 10
Example 179	< 10

Table 2-7

Test compound	IC_{50} (μM)
Example 180	< 10
Example 181	< 10
Example 182	< 10
Example 183	< 10
Example 184	< 10
Example 185	< 10
Example 186	< 10
Example 187	< 10
Example 188	< 10
Example 189	< 10
Example 190	< 10
Example 191	< 10
Example 192	< 10
Example 193	< 10
Example 194	< 10
Example 195	< 10
Example 196	< 10
Example 197	< 10
Example 198	< 10
Example 199	< 10
Example 200	< 10
Example 201	< 10
Example 202	< 10
Example 203	< 10
Example 204	< 10
Example 205	< 10
Example 206	< 10
Example 207	< 10
Example 208	< 10
Example 209	< 10
Example 210	< 10
Example 211	< 10
Example 212	< 10

Table 2-8

Test compound	IC_{50} (μM)
Example 213	< 10
Example 214	< 10
Example 215	< 10
Example 216	< 10
Example 217	< 10
Example 218	< 10
Example 219	< 10
Example 220	< 10
Example 221	< 10
Example 222	< 10
Example 223	< 10
Example 224	< 10
Example 225	< 10
Example 226	< 10
Example 227	< 10
Example 228	< 10
Example 229	< 10
Example 230	< 10
Example 231	< 10
Example 232	< 10
Example 233	< 10
Example 234	< 10
Example 235	< 10
Example 236	< 10
Example 237	< 10
Example 238	< 10
Example 239	< 10
Example 240	< 10
Example 241	< 10
Example 242	< 10
Example 243	< 10
Example 244	< 10
Example 245	< 10

Table 2-9

Test compound	IC_{50} (μM)
Example 246	< 10
Example 247	< 10
Example 248	< 10
Example 249	< 10
Example 250	< 10
Example 251	< 10
Example 252	< 10
Example 253	< 10
Example 254	< 10
Example 255	< 10
Example 256	< 10
Example 257	< 10
Example 258	< 10
Example 259	< 10
Example 260	< 10
Example 261	< 10
Example 262	< 10
Example 263	< 10
Example 264	< 10
Example 265	< 10
Example 266	< 10
Example 267	< 10
Example 268	< 10
Example 269	< 10
Example 270	< 10
Example 271	< 10
Example 272	< 10
Example 273	< 10
Example 274	< 10
Example 275	< 10
Example 276	< 10
Example 277	< 10
Example 278	< 10

Table 2-10

Test compound	IC_{50} (μM)
Example 279	< 10
Example 280	< 10
Example 281	< 10
Example 282	< 10
Example 283	< 10
Example 284	< 10
Example 285	< 10
Example 286	< 10
Example 287	< 10
Example 288	< 10
Example 289	< 10
Example 290	< 10
Example 291	< 10
Example 292	< 10
Example 293	< 10
Example 294	< 10
Example 295	< 10
Example 296	< 10
Example 297	< 10
Example 298	< 10
Example 299	< 10
Example 300	< 10
Example 301	< 10
Example 302	< 10
Example 303	< 10
Example 304	< 10
Example 305	< 10
Example 306	< 10
Example 307	< 10
Example 308	< 10
Example 309	< 10
Example 310	< 10
Example 311	< 10

Table 2-11

Test compound	IC_{50} (μM)
Example 312	< 10
Example 313	< 10
Example 314	< 10
Example 315	< 10
Example 316	< 10
Example 317	< 10
Example 318	< 10
Example 319	< 10
Example 320	< 10
Example 321	< 10
Example 322	< 10
Example 323	< 10
Example 324	< 10
Example 325	< 10
Example 326	< 10
Example 327	< 10
Example 328	< 10
Example 329	< 10
Example 330	< 10
Example 331	< 10
Example 332	< 10
Example 333	< 10
Example 334	< 10
Example 335	< 10
Example 336	< 10
Example 337	< 10
Example 338	< 10
Example 339	< 10
Example 340	< 10
Example 341	< 10
Example 342	< 10
Example 343	< 10
Example 344	< 10

Table 2-12

Test compound	IC_{50} (μM)
Example 345	< 10
Example 346	< 10
Example 347	< 10
Example 348	< 10
Example 349	< 10
Example 350	< 10
Example 351	< 10
Example 352	< 10
Example 353	< 10
Example 354	< 10
Example 355	< 10
Example 356	< 10
Example 357	< 10
Example 358	< 10
Example 359	< 10
Example 360	< 10
Example 361	< 10
Example 362	< 10
Example 363	< 10
Example 364	< 10
Example 365	< 10
Example 366	< 10
Example 367	< 10
Example 368	< 10
Example 369	< 10
Example 370	< 10
Example 371	< 10
Example 372	< 10
Example 373	< 10
Example 374	< 10
Example 375	< 10
Example 376	< 10
Example 377	< 10

Table 2-13

Test compound	IC_{50} (μM)
Example 378	< 10
Example 379	< 10
Example 380	< 10
Example 381	< 10
Example 382	< 10
Example 383	< 10
Example 384	< 10
Example 385	< 10
Example 386	< 10
Example 387	< 10
Example 388	< 10
Example 389	< 10
Example 390	< 10
Example 391	< 10
Example 392	< 10
Example 393	< 10
Example 394	< 10
Example 395	< 10
Example 396	< 10
Example 397	< 10
Example 398	< 10
Example 399	< 10
Example 400	< 10
Example 401	< 10
Example 402	< 10
Example 403	< 10
Example 404	< 10
Example 405	< 10

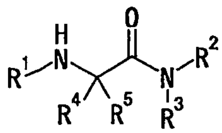
Industrial Applicability

As is clear from the Experimental Examples described above, compound [I] of the present invention has a superior DPP-IV inhibitory activity. Therefore, it is useful as a therapeutic drug for a disease involving DPP-IV, or type II diabetes, obesity and the like.

This application is based on patent application Nos. 317407/2003, 395879/2003 and 114685/2004 filed in Japan, the contents of which are hereby incorporated by reference.

Claims

1. A DPP-IV inhibitor comprising a compound represented by the formula [I]

 [I]

wherein

R^1 is selected from the following [A]-[E]:

[A] hydrogen atom,

[B] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <B1>-<B14>),

•<B1> halogen atom,

•<B2> C_{3-12} cycloalkyl,

•<B3> hydroxyl,

•<B4> C_{1-6} alkoxy,

•<B5> C_{1-6} alkylthio,

•<B6> aryloxy,

•<B7> aralkyloxy,

•<B8> heterocyclyloxy,

•<B9> heterocyclyl-C_{1-6} alkoxy,

•<B10> nitro,

•<B11> amino,

•<B12> cyano,

•<B13> carboxyl and

•<B14> $-X^1-R^{11}$ (R^{11} is selected from the following (Ba1) and (Ba2) and X^1 is selected from the following (Bb1)-(Bb23)),

••(Ba1) aryl and

••(Ba2) heterocyclyl (said aryl and heterocyclyl are optionally substituted by 1 to 3 substituents selected from the following <Baa1>-<Baa17>),

•••<Baa1> halogen atom,

•••<Baa2> C_{1-6} alkyl,

•••<Baa3> halo-C_{1-6} alkyl,

•••<Baa4> C_{3-12} cycloalkyl,

···<Baa5> aralkyl,

···<Baa6> heterocyclyl-C_{1-6} alkyl,

···<Baa7> hydroxyl,

···<Baa8> C_{1-6} alkoxy,

···<Baa9> C_{1-6} alkylthio,

···<Baa10> aryloxy,

···<Baa11> aralkyloxy,

···<Baa12> heterocyclyloxy,

···<Baa13> heterocyclyl-C_{1-6} alkoxy,

···<Baa14> nitro,

···<Baa15> amino,

···<Baa16> cyano and

···<Baa17> carboxyl;

··(Bb1) single bond,

··(Bb2) -O-,

··(Bb3) -S-,

··(Bb4) -NH-,

··(Bb5) -CO-,

··(Bb6) $-CO_2-$,

··(Bb7) -OCO-,

··(Bb8) $-OCO_2-$,

··(Bb9) -SO-,

··(Bb10) $-SO_2-$,

··(Bb11) $-OSO_2-$,

··(Bb12) $-SO_3-$,

··(Bb13) -CONH-,

··(Bb14) -NHCO-,

··(Bb15) -CSNH-,

··(Bb16) -NHCS-,

··(Bb17) $-NHSO_2-$,

··(Bb18) $-SO_2NH-$,

··(Bb19) $-NHCO_2-$,

··(Bb20) -OCONH-,

··(Bb21) -NHCONH-,

••(Bb22) -NHCSNH- and

••(Bb23) $-NHSO_2NH-$;

[C] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <C1>-<C17>),

•<C1> halogen atom,

•<C2> C_{1-6} alkyl,

•<C3> halo-C_{1-6} alkyl,

•<C4> aralkyl,

•<C5> heterocyclyl-C_{1-6} alkyl,

•<C6> hydroxyl,

•<C7> C_{1-6} alkoxy,

•<C8> C_{1-6} alkylthio,

•<C9> aryloxy,

•<C10> aralkyloxy,

•<C11> heterocyclyloxy,

•<C12> heterocyclyl-C_{1-6} alkoxy,

•<C13> nitro,

•<C14> amino,

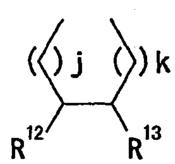
•<C15> cyano,

•<C16> carboxyl and

•<C17> $-X^1-R^{11}$ (R^{11} and X^1 are as defined above);

[D] $-X^1-R^{11}$ (R^{11} and X^1 are as defined above); or

[E]



wherein R^{12} and R^{13} are each independently selected from the following (E1)-(E3), j and k are each independently an integer of 0 to 3, which is formed by R^1 and R^4 in combination,

•(E1) hydrogen atom,

•(E2) $-X^{12}-R^{14}$ (R^{14} is selected from the following (Ea1) and (Ea2), X^{12} is selected from the following (Eb1)-(Eb24)),

••(Ea1) aryl and

··(Ea2) heterocyclyl (said aryl and heterocyclyl are optionally substituted by 1 to 3 substituents selected from the following <Eaa1>-<Eaa17>),

···<Eaa1> halogen atom,

···<Eaa2> C_{1-6} alkyl,

···<Eaa3> halo-C_{1-6} alkyl,

···<Eaa4> C_{3-12} cycloalkyl,

···<Eaa5> aralkyl,

···<Eaa6> heterocyclyl-C_{1-6} alkyl,

···<Eaa7> hydroxyl,

···<Eaa8> C_{1-6} alkoxy,

···<Eaa9> C_{1-6} alkylthio,

···<Eaa10> aryloxy,

···<Eaa11> aralkyloxy,

···<Eaa12> heterocyclyloxy,

···<Eaa13> heterocyclyl-C_{1-6} alkoxy,

···<Eaa14> nitro,

···<Eaa15> amino,

···<Eaa16> cyano and

···<Eaa17> carboxyl;

··(Eb1) single bond,

··(Eb2) -O-,

··(Eb3) -S-,

··(Eb4) -NH-,

··(Eb5) -CO-,

··(Eb6) $-CO_2-$,

··(Eb7) -OCO-,

··(Eb8) $-OCO_2-$,

··(Eb9) -SO-,

··(Eb10) $-SO_2-$,

··(Eb11) $-OSO_2-$,

··(Eb12) $-SO_3-$,

··(Eb13) -CONH-,

··(Eb14) -NHCO-,

••(Eb15) -CSNH-,

••(Eb16) -NHCS-,

••(Eb17) $-NHSO_2-$,

••(Eb18) $-SO_2NH-$,

••(Eb19) $-NHCO_2-$,

••(Eb20) -OCONH-,

••(Eb21) -NHCONH-,

••(Eb22) -NHCSNH-,

••(Eb23) $-NHSO_2NH-$ and

••(Eb24) 4 to 7-membered divalent saturated heterocycle;

or

•(E3) benzene ring formed by R^{12} and R^{13} together with the adjacent carbon atoms (said benzene ring is optionally substituted by 1 to 3 substituents selected from the following <Ec1>-<Ec17>),

••<Ec1> halogen atom,

••<Ec2> C_{1-6} alkyl,

••<Ec3> halo-C_{1-6} alkyl,

••<Ec4> C_{3-12} cycloalkyl,

••<Ec5> aralkyl,

••<Ec6> heterocyclyl-C_{1-6} alkyl,

••<Ec7> hydroxyl,

••<Ec8> C_{1-6} alkoxy,

••<Ec9> C_{1-6} alkylthio,

••<Ec10> aryloxy,

••<Ec11> aralkyloxy,

••<Ec12> heterocyclyloxy,

••<Ec13> heterocyclyl-C_{1-6} alkoxy,

••<Ec14> nitro,

••<Ec15> amino,

••<Ec16> cyano and

••<Ec17> carboxyl;

R^2 is selected from the following [F]-[H]:

[F] hydrogen atom,

[G] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3

substituents selected from the following <G1>-<G18>),

•<G1> halogen atom,

•<G2> C_{3-12} cycloalkyl,

•<G3> hydroxyl,

•<G4> C_{1-6} alkoxy,

•<G5> C_{1-6} alkylthio,

•<G6> aryloxy,

•<G7> aralkyloxy,

•<G8> heterocyclyloxy,

•<G9> heterocyclyl-C_{1-6} alkoxy,

•<G10> nitro,

•<G11> amino,

•<G12> cyano,

•<G13> amido,

•<G14> =O,

•<G15> carboxyl,

•<G16> $-PO(OH)_2$,

•<G17> $-PO(O-C_{1-6}$ alkyl$)_2$ and

•<G18> $-PO(O$-aryl$)_2$;

and

[H] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <H1>-<H21>),

•<H1> halogen atom,

•<H2> C_{1-6} alkyl,

•<H3> halo-C_{1-6} alkyl,

•<H4> aralkyl,

•<H5> heterocyclyl-C_{1-6} alkyl,

•<H6> hydroxyl,

•<H7> C_{1-6} alkoxy,

•<H8> C_{1-6} alkylthio,

•<H9> aryloxy,

•<H10> aralkyloxy,

•<H11> heterocyclyloxy,

•<H12> heterocyclyl-C_{1-6} alkoxy,

·<H13> nitro,

·<H14> amino,

·<H15> cyano,

·<H16> amido,

·<H17> =O,

·<H18> carboxyl,

·<H19> $-PO(OH)_2$,

·<H20> $-PO(O-C_{1-6}$ alkyl$)_2$ and

·<H21> $-PO(O$-aryl$)_2$;

R^3 is selected from the following [I] and [J]

[I] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <I1>-<I18>),

·<I1> halogen atom,

·<I2> C_{3-12} cycloalkyl,

·<I3> hydroxyl,

·<I4> C_{1-6} alkoxy,

·<I5> C_{1-6} alkylthio,

·<I6> aryloxy,

·<I7> aralkyloxy,

·<I8> heterocyclyloxy,

·<I9> heterocyclyl-C_{1-6} alkoxy,

·<I10> nitro,

·<I11> amino,

·<I12> cyano,

·<I13> amido,

·<I14> =O,

·<I15> carboxyl,

·<I16> $-PO(OH)_2$,

·<I17> $-PO(O-C_{1-6}$ alkyl$)_2$ and

·<I18> $-PO(O$-aryl$)_2$;

and

[J] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <J1>-<J21>),

·<J1> halogen atom,

•<J2> C_{1-6} alkyl,

•<J3> halo-C_{1-6} alkyl,

•<J4> aralkyl,

•<J5> heterocyclyl-C_{1-6} alkyl,

•<J6> hydroxyl,

•<J7> C_{1-6} alkoxy,

•<J8> C_{1-6} alkylthio,

•<J9> aryloxy,

•<J10> aralkyloxy,

•<J11> heterocyclyloxy,

•<J12> heterocyclyl-C_{1-6} alkoxy,

•<J13> nitro,

•<J14> amino,

•<J15> cyano,

•<J16> amido,

•<J17> =O,

•<J18> carboxyl,

•<J19> $-PO(OH)_2$,

•<J20> $-PO(O-C_{1-6}$ alkyl$)_2$ and

•<J21> $-PO(O$-aryl$)_2$;

R^4 is selected from the following [K]-[S]:

[K] hydrogen atom,

[L] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <L1>-<L14>),

•<L1> halogen atom,

•<L2> C_{3-12} cycloalkyl,

•<L3> hydroxyl,

•<L4> C_{1-6} alkoxy,

•<L5> C_{1-6} alkylthio,

•<L6> aryloxy,

•<L7> aralkyloxy,

•<L8> heterocyclyloxy,

•<L9> heterocyclyl-C_{1-6} alkoxy,

•<L10> nitro,

·<L11> amino,

·<L12> cyano,

·<L13> carboxyl and

·<L14> $-Y^{41}-R^{41}$ (R^{41} is selected from the following (La1)-(La8), and Y^{41} is selected from the following (Lb1) and (Lb2)),

··(La1) hydrogen atom,

··(La2) C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <Laa1>-<Laa24>),

···<Laa1> halogen atom,

···<Laa2> C_{3-12} cycloalkyl,

···<Laa3> hydroxyl,

···<Laa4> aralkyloxy,

···<Laa5> heterocyclyloxy,

···<Laa6> heterocyclyl-C_{1-6} alkoxy,

···<Laa7> nitro,

···<Laa8> cyano,

···<Laa9> carboxyl,

···<Laa10> $-OR^{413}$,

···<Laa11> $-COR^{414}$,

···<Laa12> $-CO_2R^{413}$,

···<Laa13> $-OCOR^{413}$,

···<Laa14> $-CONR^{415}R^{416}$,

···<Laa15> $-OCONR^{415}R^{416}$,

···<Laa16> $-NR^{415}R^{416}$,

···<Laa17> $-NR^{417}COR^{413}$,

···<Laa18> $-NR^{417}CO_2R^{413}$,

···<Laa19> $-SR^{413}$,

···<Laa20> $-SOR^{413}$,

···<Laa21> $-SO_2R^{413}$,

···<Laa22> $-SO_2NR^{415}R^{416}$,

···<Laa23> $-NR^{417}SO_2R^{413}$ and

···<Laa24> $-NR^{417}CONR^{415}R^{416}$

(R^{413} is C_{1-6} alkyl, C_{3-12} cycloalkyl or aryl,

R^{414}, R^{415} and R^{416} are the same or different and each is hydrogen

atom, C_{1-6} alkyl, C_{3-12} cycloalkyl or aryl,

R^{417} is hydrogen atom or C_{1-6} alkyl,

or R^{417} in combination with R^{413} form C_{1-4} alkylene);

··(La3) C_{3-12} cycloalkyl;

··(La4) C_{3-12} cycloalkyl-C_{1-6} alkyl;

··(La5) aryl;

··(La6) aralkyl;

··(La7) heterocyclyl and

··(La8) heterocyclyl-C_{1-6} alkyl

(said cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl and heterocyclylalkyl are optionally substituted by 1 to 3 substituents selected from the following <Lab1>-<Lab33>),

···<Lab1> halogen atom,

···<Lab2> C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from hydroxyl, C_{1-6} alkoxy, $-SO_2-C_{1-6}$ alkyl, $-SO_2$-aryl, $-NHSO_2-C_{1-6}$ alkyl and $-NHSO_2$-halo-C_{1-6} alkyl),

···<Lab3> halo-C_{1-6} alkyl,

···<Lab4> aralkyl,

···<Lab5> heterocyclyl-C_{1-6} alkyl,

···<Lab6> C_{3-12} cycloalkyl,

···<Lab7> hydroxyl,

···<Lab8> C_{1-6} alkoxy,

···<Lab9> aralkyloxy,

···<Lab10> heterocyclyloxy,

···<Lab11> heterocyclyl-C_{1-6} alkoxy,

···<Lab12> nitro,

···<Lab13> amino,

···<Lab14> cyano,

···<Lab15> carboxyl,

···<Lab16> (C_{1-6} alkoxy)carbonyl,

···<Lab17> C_{1-6} alkylsulfonyl,

···<Lab18> $-CH_2CO_2H$,

···<Lab19> $-OR^{413}$,

···<Lab20> $-COR^{414}$,

···<Lab21> $-CO_2R^{413}$,

···<Lab22> $-OCOR^{413}$,

···<Lab23> $-CONR^{415}R^{416}$,

···<Lab24> $-OCONR^{415}R^{416}$,

···<Lab25> $-NR^{415}R^{416}$,

···<Lab26> $-NR^{417}COR^{413}$,

···<Lab27> $-NR^{417}CO_2R^{413}$,

···<Lab28> $-SR^{413}$,

···<Lab29> $-SOR^{413}$,

···<Lab30> $-SO_2R^{413}$,

···<Lab31> $-SO_2NR^{415}R^{416}$,

···<Lab32> $-NR^{417}SO_2R^{413}$ and

···<Lab33> $-NR^{417}CONR^{415}R^{416}$

(R^{413}, R^{414}, R^{415}, R^{416} and R^{417} are as defined above);

··(Lb1) single bond and

··(Lb2) X^{41} (X^{41} is $-(CHR^{418})_c-X^{41a}-(CHR^{419})_d-$, X^{41a} is selected from the following (Lba1)-(Lba23), R^{418} and R^{419} are the same or different and each is hydrogen atom or C_{1-6} alkyl, c is an integer of 0 to 2, and d is an integer of 0 to 4),

···(Lba1) -O-,

···(Lba2) -S-,

···(Lba3) -CO-,

···(Lba4) $-CO_2-$,

···(Lba5) -OCO-,

···(Lba6) $-OCO_2-$,

···(Lba7) -SO-,

···(Lba8) $-SO_2-$,

···(Lba9) $-OSO_2-$,

···(Lba10) $-SO_3-$,

···(Lba11) $-NR^{411}-$,

···(Lba12) $-CONR^{411}-$,

···(Lba13) $-NR^{411}CO-$,

···(Lba14) $-CSNR^{411}-$,

···(Lba15) $-NR^{411}CS-$,

···(Lba16) $-SO_2NR^{411}-$,

···(Lba17) $-NR^{411}SO_2-$,

···(Lba18) $-OCONR^{411}-$,

···(Lba19) $-NR^{411}CO_2-$,

···(Lba20) $-NR^{411}CONR^{412}-$,

···(Lba21) $-NR^{411}CSNR^{412}-$,

···(Lba22) $-NR^{411}SO_2NR^{412}-$ (R^{411} and R^{412} are the same or different and each is selected from the following (Lbaa1)-(Lbaa3)),

····(Lbaa1) hydrogen atom,

····(Lbaa2) C_{1-6} alkyl (alkyl is optionally substituted by 1 to 3 substituents selected from the following <Lbaaa1>-<Lbaaa14>),

·····<Lbaaa1> halogen atom,

·····<Lbaaa2> C_{3-12} cycloalkyl,

·····<Lbaaa3> hydroxyl,

·····<Lbaaa4> C_{1-6} alkoxy,

·····<Lbaaa5> C_{1-6} alkylthio,

·····<Lbaaa6> aryloxy,

·····<Lbaaa7> aralkyloxy,

·····<Lbaaa8> heterocyclyloxy,

·····<Lbaaa9> heterocyclyl-C_{1-6} alkoxy,

·····<Lbaaa10> nitro,

·····<Lbaaa11> amino,

·····<Lbaaa12> cyano,

·····<Lbaaa13> carboxyl,

·····<Lbaaa14> oxo; and

····(Lbaa3) $-(CH_2)_p-$ (p is an integer of 1 to 3) formed by R^{411} and R^{412} in combination; and

···(Lba23) 4 to 7-membered divalent saturated heterocycle;

[M] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <M1>-<M18>),

·<M1> halogen atom,

·<M2> C_{1-6} alkyl,

·<M3> halo-C_{1-6} alkyl,

·<M4> aralkyl,

•<M5> heterocyclyl-C_{1-6} alkyl,

•<M6> hydroxyl,

•<M7> C_{1-6} alkoxy,

•<M8> C_{1-6} alkylthio,

•<M9> aryloxy,

•<M10> aralkyloxy,

•<M11> heterocyclyloxy,

•<M12> heterocyclyl-C_{1-6} alkoxy,

•<M13> azido,

•<M14> nitro,

•<M15> amino,

•<M16> cyano,

•<M17> carboxyl and

•<M18> $-Y^{42}-R^{41}$ (R^{41} is as defined above, and Y^{42} is selected from the following (Ma1)-(Ma12)),

••(Ma1) single bond,

••(Ma2) $-X^{41}-$,

••(Ma3) $-Z^{41}-$,

••(Ma4) $-Z^{41}-Z^{42}-$,

••(Ma5) $-X^{41}-Z^{41}-$,

••(Ma6) $-Z^{41}-X^{41}-$,

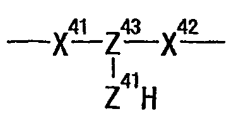
••(Ma7) $-X^{41}-Z^{41}-X^{42}-$,

••(Ma8) $-X^{41}-Z^{41}-Z^{42}-$,

••(Ma9) $-Z^{41}-X^{41}-Z^{42}-$,

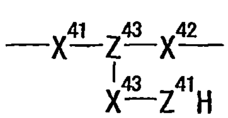
••(Ma10) $-Z^{41}-Z^{42}-X^{41}-$,

••(Ma11)



and

••(Ma12)



(X^{41} is as defined above, X^{42} and X^{43} are each independently $-(CHR^{420})_e-X^{42a}-(CHR^{421})_f-$, X^{42a} is selected from the following (Maa1)-(Maa23), R^{420} and R^{421} are the same or different and each is hydrogen atom or C_{1-6} alkyl, e and f are each independently an integer of 0 to 2, Z^{41} and Z^{42} are the same or different and each is selected from the following (Mab1)-(Mab6), and Z^{43} is selected from the following (Mac1)-(Mac5)),

•••(Maa1) single bond,

•••(Maa2) –O–,

•••(Maa3) –S–,

•••(Maa4) –CO–,

•••(Maa5) $-CO_2-$,

•••(Maa6) –OCO–,

•••(Maa7) $-OCO_2-$,

•••(Maa8) –SO–,

•••(Maa9) $-SO_2-$,

•••(Maa10) $-OSO_2-$,

•••(Maa11) $-SO_3-$,

•••(Maa12) $-NR^{411}-$,

•••(Maa13) $-CONR^{411}-$,

•••(Maa14) $-NR^{411}CO-$,

•••(Maa15) $-NR^{411}CO_2-$,

•••(Maa16) $-OCONR^{411}-$,

•••(Maa17) $-CSNR^{411}-$,

•••(Maa18) $-NR^{411}CS-$,

•••(Maa19) $-SO_2NR^{411}-$,

•••(Maa20) $-NR^{411}SO_2-$,

•••(Maa21) $-NR^{411}CONR^{412}-$,

•••(Maa22) $-NR^{411}CSNR^{412}-$ and

•••(Maa23) $-NR^{411}SO_2NR^{412}-$ (R^{411} and R^{412} are as defined above);

•••(Mab1) C_{1-6} alkylene,

•••(Mab2) C_{2-6} alkenylene,

•••(Mab3) C_{2-6} alkynylene (said alkylene, alkenylene and alkynylene are optionally substituted by 1 to 3 substituents selected from

the following <Maba1>-<Maba13>),

····<Maba1> halogen atom,

····<Maba2> C_{3-12} cycloalkyl,

····<Maba3> hydroxyl,

····<Maba4> C_{1-6} alkoxy,

····<Maba5> C_{1-6} alkylthio,

····<Maba6> aryloxy,

····<Maba7> aralkyloxy,

····<Maba8> heterocyclyloxy,

····<Maba9> heterocyclyl-C_{1-6} alkoxy,

····<Maba10> nitro,

····<Maba11> amino,

····<Maba12> cyano and

····<Maba13> carboxyl;

···(Mab4) C_{3-12} cycloalkylene,

···(Mab5) arylene and

···(Mab6) divalent heterocycle (said cycloalkylene, arylene and heterocycle are optionally substituted by 1 to 3 substituents selected from the following <Mabb1>-<Mabb18>),

····<Mabb1> halogen atom,

····<Mabb2> C_{1-6} alkyl,

····<Mabb3> halo-C_{1-6} alkyl,

····<Mabb4> aralkyl,

····<Mabb5> heterocyclyl-C_{1-6} alkyl,

····<Mabb6> C_{3-12} cycloalkyl,

····<Mabb7> hydroxyl,

····<Mabb8> C_{1-6} alkoxy,

····<Mabb9> C_{1-6} alkylthio,

····<Mabb10> aryloxy,

····<Mabb11> aralkyloxy,

····<Mabb12> heterocyclyloxy,

····<Mabb13> heterocyclyl-C_{1-6} alkoxy,

····<Mabb14> nitro,

····<Mabb15> amino,

····<Mabb16> cyano,

····<Mabb17> carboxyl and

····<Mabb18> $-X^{4c}-R^{4c}$ (R^{4c} is selected from the following (Mabba1)-(Mabba4), and X^{4c} is selected from the following (Mabbb1)-(Mabbb9)),

·····(Mabba1) hydrogen atom,

·····(Mabba2) C_{1-6} alkyl,

·····(Mabba3) aryl and

·····(Mabba4) aralkyl (alkyl, aryl and aralkyl are optionally substituted by 1 to 3 substituents selected from the following <Mabbaa1>-<Mabbaa4>)

······<Mabbaa1> halogen atom,

······<Mabbaa2> carboxyl,

······<Mabbaa3> (C_{1-6} alkoxy)carbonyl and

······<Mabbaa4> C_{1-6} alkylsulfonyl;

·····(Mabbb1) single bond,

·····(Mabbb2) $-CO-$,

·····(Mabbb3) $-CO_2-$,

·····(Mabbb4) $-OCO-$,

·····(Mabbb5) $-CONR^{41c}-$,

·····(Mabbb6) $-NR^{41c}CO-$,

·····(Mabbb7) $-SO_2-$,

·····(Mabbb8) $-SO_2NR^{41c}-$ and

·····(Mabbb9) $-NR^{41c}SO_2-$ (R^{41c} is hydrogen atom or C_{1-6} alkyl);

···(Mac1) C_{1-6} alkanetriyl,

···(Mac2) C_{2-6} alkenetriyl (said alkanetriyl and alkenetriyl are optionally substituted by 1 to 3 substituents selected from the following <Maca1>-<Maca13>)

····<Maca1> halogen atom,

····<Maca2> C_{3-12} cycloalkyl,

····<Maca3> hydroxyl,

····<Maca4> C_{1-6} alkoxy,

····<Maca5> C_{1-6} alkylthio,

····<Maca6> aryloxy,

····<Maca7> aralkyloxy,

····<Maca8> heterocyclyloxy,

····<Maca9> heterocyclyl-C_{1-6} alkoxy,

····<Maca10> nitro,

····<Maca11> amino,

····<Maca12> cyano and

····<Maca13> carboxyl;

···(Mac3) C_{3-12} cycloalkanetriyl,

···(Mac4) arenetriyl and

···(Mac5) trivalent heterocycle (said cycloalkanetriyl, arenetriyl and heterocycle are optionally substituted by 1 to 3 substituents selected from the following <Macb1>-<Macb18>),

····<Macb1> halogen atom,

····<Macb2> C_{1-6} alkyl,

····<Macb3> halo-C_{1-6} alkyl,

····<Macb4> aralkyl,

····<Macb5> heterocyclyl-C_{1-6} alkyl,

····<Macb6> C_{3-12} cycloalkyl,

····<Macb7> hydroxyl,

····<Macb8> C_{1-6} alkoxy,

····<Macb9> C_{1-6} alkylthio,

····<Macb10> aryloxy,

····<Macb11> aralkyloxy,

····<Macb12> heterocyclyloxy,

····<Macb13> heterocyclyl-C_{1-6} alkoxy,

····<Macb14> nitro,

····<Macb15> amino,

····<Macb16> cyano,

····<Macb17> carboxyl and

····<Macb18> $-CH_2CO_2H$;

[N] aryl,

[O] aralkyl,

[P] heterocyclyl,

[Q] heterocyclyl-C_{1-6} alkyl (said aryl, aralkyl, heterocyclyl and heterocyclyl-C_{1-6} alkyl are optionally substituted by 1 to 3

substituents selected from the following <N1>-<N19>),

•<N1> halogen atom,

•<N2> C_{1-6} alkyl,

•<N3> C_{3-12} cycloalkyl,

•<N4> halo-C_{1-6} alkyl,

•<N5> aralkyl,

•<N6> heterocyclyl-C_{1-6} alkyl,

•<N7> hydroxyl,

•<N8> C_{1-6} alkoxy,

•<N9> C_{1-6} alkylthio,

•<N10> aryloxy,

•<N11> aralkyloxy,

•<N12> heterocyclyloxy,

•<N13> heterocyclyl-C_{1-6} alkoxy,

•<N14> nitro,

•<N15> amino,

•<N16> cyano,

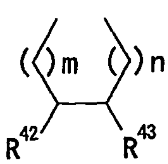
•<N17> =O,

•<N18> carboxyl and

•<N19> $-Y^{42}-R^{41}$ (R^{41} and Y^{42} are as defined above);

[R] $-Y^{41}-R^{41}$ (R^{41} and Y^{41} are as defined above), or

[S]



(R^{42} and R^{43} are each independently selected from the following (S1)-(S3), and m and n are each independently an integer of 0 to 3) formed by R^4 and R^5 in combination,

•(S1) hydrogen atom,

•(S2) $-Y^{41}-R^{44}$ (R^{44} is selected from the following (Sa1) and (Sa2) and Y^{41} are as defined above),

••(Sa1) aryl and

••(Sa2) heterocyclyl (aryl and heterocyclyl are optionally

substituted by 1 to 3 substituents selected from the following <Saa1>-<Saa17>),

···<Saa1> halogen atom,

···<Saa2> C_{1-6} alkyl,

···<Saa3> halo-C_{1-6} alkyl,

···<Saa4> aralkyl,

···<Saa5> heterocyclyl-C_{1-6} alkyl,

···<Saa6> C_{3-12} cycloalkyl,

···<Saa7> hydroxyl,

···<Saa8> C_{1-6} alkoxy,

···<Saa9> C_{1-6} alkylthio,

···<Saa10> aryloxy,

···<Saa11> aralkyloxy,

···<Saa12> heterocyclyloxy,

···<Saa13> heterocyclyl-C_{1-6} alkoxy,

···<Saa14> nitro,

···<Saa15> amino,

···<Saa16> cyano and

···<Saa17> carboxyl;

or

·(S3) benzene ring formed by R^{42} and R^{43} together with the adjacent carbon atoms (said benzene ring is optionally substituted by 1 to 3 substituents selected from the following <Sc1>-<Sc17>),

··<Sc1> halogen atom,

··<Sc2> C_{1-6} alkyl,

··<Sc3> halo-C_{1-6} alkyl,

··<Sc4> aralkyl,

··<Sc5> heterocyclyl-C_{1-6} alkyl,

··<Sc6> C_{3-12} cycloalkyl,

··<Sc7> hydroxyl,

··<Sc8> C_{1-6} alkoxy,

··<Sc9> C_{1-6} alkylthio,

··<Sc10> aryloxy,

··<Sc11> aralkyloxy,

··<Sc12> heterocyclyloxy,

··<Sc13> heterocyclyl-C_{1-6} alkoxy,

··<Sc14> nitro,

··<Sc15> amino,

··<Sc16> cyano and

··<Sc17> carboxyl;

R^5 is selected from the following [T]-[BB],

[T] hydrogen atom,

[U] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <U1>-<U14>),

·<U1> halogen atom,

·<U2> C_{3-12} cycloalkyl,

·<U3> hydroxyl,

·<U4> C_{1-6} alkoxy,

·<U5> C_{1-6} alkylthio,

·<U6> aryloxy,

·<U7> aralkyloxy,

·<U8> heterocyclyloxy,

·<U9> heterocyclyl-C_{1-6} alkoxy,

·<U10> nitro,

·<U11> amino,

·<U12> cyano,

·<U13> carboxyl and

·<U14> $-X^{44}-R^{45}$ (R^{45} is selected from the following (Ua1) and (Ua2), and X^{44} is selected from the following (Ub1)-(Ub23)),

··(Ua1) aryl and

··(Ua2) heterocyclyl (said aryl and heterocyclyl are optionally substituted by 1 to 3 substituents selected from the following <Uaa1>-<Uaa17>)

···<Uaa1> halogen atom,

···<Uaa2> C_{1-6} alkyl,

···<Uaa3> halo-C_{1-6} alkyl,

···<Uaa4> C_{3-12} cycloalkyl,

···<Uaa5> aralkyl,

・・・<Uaa6> heterocyclyl-C_{1-6} alkyl,

・・・<Uaa7> hydroxyl,

・・・<Uaa8> C_{1-6} alkoxy,

・・・<Uaa9> C_{1-6} alkylthio,

・・・<Uaa10> aryloxy,

・・・<Uaa11> aralkyloxy,

・・・<Uaa12> heterocyclyloxy,

・・・<Uaa13> heterocyclyl-C_{1-6} alkoxy,

・・・<Uaa14> nitro,

・・・<Uaa15> amino,

・・・<Uaa16> cyano and

・・・<Uaa17> carboxyl;

・・(Ub1) single bond,

・・(Ub2) -O-,

・・(Ub3) -S-,

・・(Ub4) -NH-,

・・(Ub5) -CO-,

・・(Ub6) -CO_2-,

・・(Ub7) -OCO-,

・・(Ub8) -OCO_2-,

・・(Ub9) -SO-,

・・(Ub10) -SO_2-,

・・(Ub11) -OSO_2-,

・・(Ub12) -SO_3-,

・・(Ub13) -CONH-,

・・(Ub14) -NHCO-,

・・(Ub15) -CSNH-,

・・(Ub16) -NHCS-,

・・(Ub17) -$NHSO_2$-,

・・(Ub18) -SO_2NH-,

・・(Ub19) -$NHCO_2$-,

・・(Ub20) -OCONH-,

・・(Ub21) -NHCONH-,

・・(Ub22) -NHCSNH- and

••(Ub23) $-NHSO_2NH-$;

[V] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <V1>-<V17>),

•<V1> halogen atom,

•<V2> C_{1-6} alkyl,

•<V3> halo-C_{1-6} alkyl,

•<V4> aralkyl,

•<V5> heterocyclyl-C_{1-6} alkyl,

•<V6> hydroxyl,

•<V7> C_{1-6} alkoxy,

•<V8> C_{1-6} alkylthio,

•<V9> aryloxy,

•<V10> aralkyloxy,

•<V11> heterocyclyloxy,

•<V12> heterocyclyl-C_{1-6} alkoxy,

•<V13> nitro,

•<V14> amino,

•<V15> cyano,

•<V16> carboxyl and

•<V17> $-X^{44}-R^{45}$ (R^{45} and X^{44} are as defined above);

[W] 3 to 7-membered saturated heterocycle,

[X] aryl,

[Y] heterocyclyl,

[Z] aralkyl,

[AA] heterocyclyl-C_{1-6} alkyl (said saturated heterocycle, aryl, heterocyclyl, aralkyl and heterocyclyl-C_{1-6} alkyl are optionally substituted by 1 to 3 substituents selected from the following <W1>-<W16>),

•<W1> halogen atom,

•<W2> C_{1-6} alkyl,

•<W3> C_{3-12} cycloalkyl,

•<W4> aralkyl,

•<W5> heterocyclyl-C_{1-6} alkyl,

•<W6> hydroxyl,

·<W7> C_{1-6} alkoxy,

·<W8> C_{1-6} alkylthio,

·<W9> aryloxy,

·<W10> aralkyloxy,

·<W11> heterocyclyloxy,

·<W12> heterocyclyl-C_{1-6} alkoxy,

·<W13> nitro,

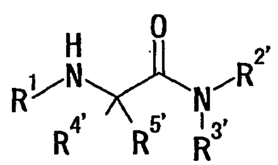
·<W14> amino,

·<W15> cyano and

·<W16> carboxyl; and

[BB] $-X^{44}-R^{45}$ (R^{45} and X^{44} are as defined above), or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

2. A compound represented by the formula [II]



[II]

wherein R^1 is selected from the following [A]-[E]:

[A] hydrogen atom,

[B] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <B1>-<B14>),

·<B1> halogen atom,

·<B2> C_{3-12} cycloalkyl,

·<B3> hydroxyl,

·<B4> C_{1-6} alkoxy,

·<B5> C_{1-6} alkylthio,

·<B6> aryloxy,

·<B7> aralkyloxy,

·<B8> heterocyclyloxy,

·<B9> heterocyclyl-C_{1-6} alkoxy,

·<B10> nitro,

·<B11> amino,

•<B12> cyano,

•<B13> carboxyl and

•<B14> $-X^1-R^{11}$ (R^{11} and X^1 are defined in claim 1);

[C] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <C1>-<C17>),

•<C1> halogen atom,

•<C2> C_{1-6} alkyl,

•<C3> halo-C_{1-6} alkyl,

•<C4> aralkyl,

•<C5> heterocyclyl-C_{1-6} alkyl,

•<C6> hydroxyl,

•<C7> C_{1-6} alkoxy,

•<C8> C_{1-6} alkylthio,

•<C9> aryloxy,

•<C10> aralkyloxy,

•<C11> heterocyclyloxy,

•<C12> heterocyclyl-C_{1-6} alkoxy,

•<C13> nitro,

•<C14> amino,

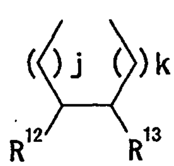
•<C15> cyano,

•<C16> carboxyl and

•<C17> $-X^1-R^{11}$ (R^{11} and X^1 are as defined in claim 1);

[D] $-X^1-R^{11}$ (R^{11} and X^1 are as defined in claim 1); or

[E]



wherein R^{12}, R^{13}, j and k are as defined in claim 1, which is formed by R^1 and $R^{4'}$ in combination;

$R^{2'}$ is selected from the following [F]-[H],

[F] hydrogen atom,

[G] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <G1>-<G18>),

- <G1> halogen atom,
- <G2> C_{3-12} cycloalkyl,
- <G3> hydroxyl,
- <G4> C_{1-6} alkoxy,
- <G5> C_{1-6} alkylthio,
- <G6> aryloxy,
- <G7> aralkyloxy,
- <G8> heterocyclyloxy,
- <G9> heterocyclyl-C_{1-6} alkoxy,
- <G10> nitro,
- <G11> amino,
- <G12> cyano,
- <G13> amido,
- <G14> =O,
- <G15> carboxyl,
- <G16> $-PO(OH)_2$,
- <G17> $-PO(O-C_{1-6}$ alkyl$)_2$ and
- <G18> $-PO(O$-aryl$)_2$;

[H] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <H1>-<H16> and <H18>-<H21>),

- <H1> halogen atom,
- <H2> C_{1-6} alkyl,
- <H3> halo-C_{1-6} alkyl,
- <H4> aralkyl,
- <H5> heterocyclyl-C_{1-6} alkyl,
- <H6> hydroxyl,
- <H7> C_{1-6} alkoxy,
- <H8> C_{1-6} alkylthio,
- <H9> aryloxy,
- <H10> aralkyloxy,
- <H11> heterocyclyloxy,
- <H12> heterocyclyl-C_{1-6} alkoxy,
- <H13> nitro,

•<H14> amino,

•<H15> cyano,

•<H16> amido,

•<H18> carboxyl,

•<H19> $-PO(OH)_2$,

•<H20> $-PO(O-C_{1-6}$ alkyl$)_2$ and

•<H21> $-PO(O$-aryl$)_2$;

$R^{3'}$ is the following [J]

[J] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <J1>-<J16> and <J18>-<J21>),

•<J1> halogen atom,

•<J2> C_{1-6} alkyl,

•<J3> halo-C_{1-6} alkyl,

•<J4> aralkyl,

•<J5> heterocyclyl-C_{1-6} alkyl,

•<J6> hydroxyl,

•<J7> C_{1-6} alkoxy,

•<J8> C_{1-6} alkylthio,

•<J9> aryloxy,

•<J10> aralkyloxy,

•<J11> heterocyclyloxy,

•<J12> heterocyclyl-C_{1-6} alkoxy,

•<J13> nitro,

•<J14> amino,

•<J15> cyano,

•<J16> amido,

•<J18> carboxyl,

•<J19> $-PO(OH)_2$,

•<J20> $-PO(O-C_{1-6}$ alkyl$)_2$ and

•<J21> $-PO(O$-aryl$)_2$;

$R^{4'}$ is selected from the following [K]-[M], [P], [R] and [S],

[K] hydrogen atom,

[L] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3

substituents selected from the following <L1>-<L14>)

·<L1> halogen atom,

·<L2> C_{3-12} cycloalkyl,

·<L3> hydroxyl,

·<L4> C_{1-6} alkoxy,

·<L5> C_{1-6} alkylthio,

·<L6> aryloxy,

·<L7> aralkyloxy,

·<L8> heterocyclyloxy,

·<L9> heterocyclyl-C_{1-6} alkoxy,

·<L10> nitro,

·<L11> amino,

·<L12> cyano,

·<L13> carboxyl and

·<L14> $-Y^{41}-R^{41'}$ ($R^{41'}$ is selected from the following (La1), (La2), (La5) and (La7), and Y^{41} is as defined in claim 1),

··(La1) hydrogen atom,

··(La2) C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <Laa1>-<Laa24>),

···<Laa1> halogen atom,

···<Laa2> C_{3-12} cycloalkyl,

···<Laa3> hydroxyl,

···<Laa4> aralkyloxy,

···<Laa5> heterocyclyloxy,

···<Laa6> heterocyclyl-C_{1-6} alkoxy,

···<Laa7> nitro,

···<Laa8> cyano,

···<Laa9> carboxyl,

···<Laa10> $-OR^{413}$,

···<Laa11> $-COR^{414}$,

···<Laa12> $-CO_2R^{413}$,

···<Laa13> $-OCOR^{413}$,

···<Laa14> $-CONR^{415}R^{416}$,

···<Laa15> $-OCONR^{415}R^{416}$,

···<Laa16> $-NR^{415}R^{416}$,

···<Laa17> $-NR^{417}COR^{413}$,

···<Laa18> $-NR^{417}CO_2R^{413}$,

···<Laa19> $-SR^{413}$,

···<Laa20> $-SOR^{413}$,

···<Laa21> $-SO_2R^{413}$,

···<Laa22> $-SO_2NR^{415}R^{416}$,

···<Laa23> $-NR^{417}SO_2R^{413}$ and

···<Laa24> $-NR^{417}CONR^{415}R^{416}$

(R^{413}, R^{414}, R^{415}, R^{416} and R^{417} is as defined in claim 1);

··(La5) aryl and

··(La7) heterocyclyl (said aryl and heterocyclyl are optionally substituted by 1 to 3 substituents selected from the following <Lab1>-<Lab33>),

···<Lab1> halogen atom,

···<Lab2> C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from hydroxyl, C_{1-6} alkoxy, $-SO_2-C_{1-6}$ alkyl, $-SO_2-$ aryl, $-NHSO_2-C_{1-6}$ alkyl and $-NHSO_2$-halo-C_{1-6} alkyl),

···<Lab3> halo-C_{1-6} alkyl,

···<Lab4> aralkyl,

···<Lab5> heterocyclyl-C_{1-6} alkyl,

···<Lab6> C_{3-12} cycloalkyl,

···<Lab7> hydroxyl,

···<Lab8> C_{1-6} alkoxy,

···<Lab9> aralkyloxy,

···<Lab10> heterocyclyloxy,

···<Lab11> heterocyclyl-C_{1-6} alkoxy,

···<Lab12> nitro,

···<Lab13> amino,

···<Lab14> cyano,

···<Lab15> carboxyl,

···<Lab16> (C_{1-6} alkoxy)carbonyl,

···<Lab17> C_{1-6} alkylsulfonyl,

···<Lab18> $-CH_2CO_2H$,

···<Lab19> $-OR^{413}$,

···<Lab20> $-COR^{414}$,

···<Lab21> $-CO_2R^{413}$,

···<Lab22> $-OCOR^{413}$,

···<Lab23> $-CONR^{415}R^{416}$,

···<Lab24> $-OCONR^{415}R^{416}$,

···<Lab25> $-NR^{415}R^{416}$,

···<Lab26> $-NR^{417}COR^{413}$,

···<Lab27> $-NR^{417}CO_2R^{413}$,

···<Lab28> $-SR^{413}$,

···<Lab29> $-SOR^{413}$,

···<Lab30> $-SO_2R^{413}$,

···<Lab31> $-SO_2NR^{415}R^{416}$,

···<Lab32> $-NR^{417}SO_2R^{413}$ and

···<Lab33> $-NR^{417}CONR^{415}R^{416}$

(R^{413}, R^{414}, R^{415}, R^{416} and R^{417} are as defined in claim 1);

[M] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <M1>-<M18>),

·<M1> halogen atom,

·<M2> C_{1-6} alkyl,

·<M3> halo-C_{1-6} alkyl,

·<M4> aralkyl,

·<M5> heterocyclyl-C_{1-6} alkyl,

·<M6> hydroxyl,

·<M7> C_{1-6} alkoxy,

·<M8> C_{1-6} alkylthio,

·<M9> aryloxy,

·<M10> aralkyloxy,

·<M11> heterocyclyloxy,

·<M12> heterocyclyl-C_{1-6} alkoxy,

·<M13> azido,

·<M14> nitro,

·<M15> amino,

·<M16> cyano,

•<M17> carboxyl and

•<M18> $-Y^{42}-R^{41'}$ ($R^{41'}$ is as defined above and Y^{42} is as defined in the claim 1);

[P] 3 to 7-membered saturated heterocycle (said saturated heterocycle is optionally substituted by 1 to 3 substituents selected from the following <N1>-<N16> and <N18>),

•<N1> halogen atom,

•<N2> C_{1-6} alkyl,

•<N3> C_{3-12} cycloalkyl,

•<N4> halo-C_{1-6} alkyl,

•<N5> aralkyl,

•<N6> heterocyclyl-C_{1-6} alkyl,

•<N7> hydroxyl,

•<N8> C_{1-6} alkoxy,

•<N9> C_{1-6} alkylthio,

•<N10> aryloxy,

•<N11> aralkyloxy,

•<N12> heterocyclyloxy,

•<N13> heterocyclyl-C_{1-6} alkoxy,

•<N14> nitro,

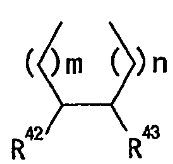
•<N15> amino,

•<N16> cyano and

•<N18> carboxyl;

[R] $-Y^{41}-R^{41'}$ ($R^{41'}$ and Y^{41} are as defined above), or

[S]



(R^{42} and R^{43} are each as defined in claim 1, m and n are each independently an integer of 0 to 3) formed by $R^{4'}$ and $R^{5'}$ in combination,

$R^{5'}$ is selected from the following [T]-[W] and [BB],

[T] hydrogen atom,

[U] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <U1>-<U14>),

·<U1> halogen atom,

·<U2> C_{3-12} cycloalkyl,

·<U3> hydroxyl,

·<U4> C_{1-6} alkoxy,

·<U5> C_{1-6} alkylthio,

·<U6> aryloxy,

·<U7> aralkyloxy,

·<U8> heterocyclyloxy,

·<U9> heterocyclyl-C_{1-6} alkoxy,

·<U10> nitro,

·<U11> amino,

·<U12> cyano,

·<U13> carboxyl and

·<U14> $-X^{44}-R^{45}$ (R^{45} and X^{44} are as defined in claim 1);

[V] C_{3-12} cycloalkyl (cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <V1>-<V17>),

·<V1> halogen atom,

·<V2> C_{1-6} alkyl,

·<V3> halo-C_{1-6} alkyl,

·<V4> aralkyl,

·<V5> heterocyclyl-C_{1-6} alkyl,

·<V6> hydroxyl,

·<V7> C_{1-6} alkoxy,

·<V8> C_{1-6} alkylthio,

·<V9> aryloxy,

·<V10> aralkyloxy,

·<V11> heterocyclyloxy,

·<V12> heterocyclyl-C_{1-6} alkoxy,

·<V13> nitro,

·<V14> amino,

·<V15> cyano,

·<V16> carboxyl and

•<V17> $-X^{44}-R^{45}$ (R^{45} and X^{44} are as defined in claim 1);

[W] 3 to 7-membered saturated heterocycle (said saturated heterocycle is optionally substituted by 1 to 3 substituents selected from the following <W1>-<W16>),

•<W1> halogen atom,

•<W2> C_{1-6} alkyl,

•<W3> C_{3-12} cycloalkyl,

•<W4> aralkyl,

•<W5> heterocyclyl-C_{1-6} alkyl,

•<W6> hydroxyl,

•<W7> C_{1-6} alkoxy,

•<W8> C_{1-6} alkylthio,

•<W9> aryloxy,

•<W10> aralkyloxy,

•<W11> heterocyclyloxy,

•<W12> heterocyclyl-C_{1-6} alkoxy,

•<W13> nitro,

•<W14> amino,

•<W15> cyano and

•<W16> carboxyl;

[BB] $-X^{44}-R^{45}$ (R^{45} and X^{44} are as defined in claim 1), provided that, when R^1 and $R^{2'}$ are hydrogen atoms and $R^{3'}$ is cyclopropyl, then the combination of one of $R^{4'}$ and $R^{5'}$ being isopropyl or tert-butyl, and the other being hydrogen atom does not occur, and when R^1 and $R^{2'}$ are hydrogen atoms and $R^{3'}$ is cyclobutyl, then the combination of one of $R^{4'}$ and $R^{5'}$ being tert-butyl, and the other being hydrogen atom does not occur,

or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

3. The compound of claim 2, wherein $R^{41'}$ is selected from the following (La1), (La2), (La5) and (La7), X^{41a} is selected from the following (Lba1)-(Lba23), and other symbols are as defined in claim 2,

••(La1) hydrogen atom,

••(La2) C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <Laa1>-<Laa24>),

•••<Laa1> halogen atom,

•••<Laa2> C_{3-12} cycloalkyl,

•••<Laa3> hydroxyl,

•••<Laa4> aralkyloxy,

•••<Laa5> heterocyclyloxy,

•••<Laa6> heterocyclyl-C_{1-6} alkoxy,

•••<Laa7> nitro,

•••<Laa8> cyano,

•••<Laa9> carboxyl,

•••<Laa10> $-OR^{413}$,

•••<Laa11> $-COR^{414}$,

•••<Laa12> $-CO_2R^{413}$,

•••<Laa13> $-OCOR^{413}$,

•••<Laa14> $-CONR^{415}R^{416}$,

•••<Laa15> $-OCONR^{415}R^{416}$,

•••<Laa16> $-NR^{415}R^{416}$,

•••<Laa17> $-NR^{417}COR^{413}$,

•••<Laa18> $-NR^{417}CO_2R^{413}$,

•••<Laa19> $-SR^{413}$,

•••<Laa20> $-SOR^{413}$,

•••<Laa21> $-SO_2R^{413}$,

•••<Laa22> $-SO_2NR^{415}R^{416}$,

•••<Laa23> $-NR^{417}SO_2R^{413}$ and

•••<Laa24> $-NR^{417}CONR^{415}R^{416}$

(R^{413} is C_{1-6} alkyl, C_{3-12} cycloalkyl or aryl,

R^{414}, R^{415} and R^{416} are the same or different and each is hydrogen atom, C_{1-6} alkyl, C_{3-12} cycloalkyl or aryl,

R^{417} is hydrogen atom or C_{1-6} alkyl);

••(La5) aryl and

••(La7) heterocyclyl (said aryl and heterocyclyl are optionally substituted by 1 to 3 substituents selected from the following

<Lab1>-<Lab33>),

···<Lab1> halogen atom,

···<Lab2> C_{1-6} alkyl,

···<Lab3> halo-C_{1-6} alkyl,

···<Lab4> aralkyl,

···<Lab5> heterocyclyl-C_{1-6} alkyl,

···<Lab6> C_{3-12} cycloalkyl,

···<Lab7> hydroxyl,

···<Lab8> C_{1-6} alkoxy,

···<Lab9> aralkyloxy,

···<Lab10> heterocyclyloxy,

···<Lab11> heterocyclyl-C_{1-6} alkoxy,

···<Lab12> nitro,

···<Lab13> amino,

···<Lab14> cyano,

···<Lab15> carboxyl,

···<Lab16> (C_{1-6} alkoxy)carbonyl,

···<Lab17> C_{1-6} alkylsulfonyl,

···<Lab18> $-CH_2CO_2H$,

···<Lab19> $-OR^{413}$,

···<Lab20> $-COR^{414}$,

···<Lab21> $-CO_2R^{413}$,

···<Lab22> $-OCOR^{413}$,

···<Lab23> $-CONR^{415}R^{416}$,

···<Lab24> $-OCONR^{415}R^{416}$,

···<Lab25> $-NR^{415}R^{416}$,

···<Lab26> $-NR^{417}COR^{413}$,

···<Lab27> $-NR^{417}CO_2R^{413}$,

···<Lab28> $-SR^{413}$,

···<Lab29> $-SOR^{413}$,

···<Lab30> $-SO_2R^{413}$,

···<Lab31> $-SO_2NR^{415}R^{416}$,

···<Lab32> $-NR^{417}SO_2R^{413}$ and

···<Lab33> $-NR^{417}CONR^{415}R^{416}$

(R^{413}, R^{414}, R^{415}, R^{416} and R^{417} are as defined above);

···(Lba1) -O-,

···(Lba2) -S-,

···(Lba3) -CO-,

···(Lba4) $-CO_2-$,

···(Lba5) -OCO-,

···(Lba6) $-OCO_2-$,

···(Lba7) -SO-,

···(Lba8) $-SO_2-$,

···(Lba9) $-OSO_2-$,

···(Lba10) $-SO_3-$,

···(Lba11) $-NR^{411}-$,

···(Lba12) $-CONR^{411}-$,

···(Lba13) $-NR^{411}CO-$,

···(Lba14) $-CSNR^{411}-$,

···(Lba15) $-NR^{411}CS-$,

···(Lba16) $-SO_2NR^{411}-$,

···(Lba17) $-NR^{411}SO_2-$,

···(Lba18) $-OCONR^{411}-$,

···(Lba19) $-NR^{411}CO_2-$,

···(Lba20) $-NR^{411}CONR^{412}-$,

···(Lba21) $-NR^{411}CSNR^{412}-$,

···(Lba22) $-NR^{411}SO_2NR^{412}-$ (R^{411} and R^{412} are the same or different and each is selected from the following (Lbaa1)-(Lbaa3)),

····(Lbaa1) hydrogen atom,

····(Lbaa2) C_{1-6} alkyl (alkyl is optionally substituted by 1 to 3 substituents selected from the following <Lbaaa1>-<Lbaaa13>),

·····<Lbaaa1> halogen atom,

·····<Lbaaa2> C_{3-12} cycloalkyl,

·····<Lbaaa3> hydroxyl,

·····<Lbaaa4> C_{1-6} alkoxy,

·····<Lbaaa5> C_{1-6} alkylthio,

·····<Lbaaa6> aryloxy,

·····<Lbaaa7> aralkyloxy,

·····<Lbaaa8> heterocyclyloxy,

·····<Lbaaa9> heterocyclyl-C_{1-6} alkoxy,

·····<Lbaaa10> nitro,

·····<Lbaaa11> amino,

·····<Lbaaa12> cyano,

·····<Lbaaa13> carboxyl, and

····(Lbaa3) $-(CH_2)_p-$ (p is an integer of 1 to 3) formed by R^{411} and R^{412} in combination; and

···(Lba23) 4 to 7-membered divalent saturated heterocycle,

or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

4. The compound of claim 2, wherein R^1 is

[A] hydrogen atom,

[B] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <B1>-<B4>, <B10>-<B12> and <B14>),

·<B1> halogen atom,

·<B2> C_{3-12} cycloalkyl,

·<B3> hydroxyl,

·<B4> C_{1-6} alkoxy,

·<B10> nitro,

·<B11> amino,

·<B12> cyano and

·<B14> $-X^1-R^{11}$ (R^{11} and X^1 are each as defined in claim 1); or

[C] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <C1>, <C2>, <C6>, <C7> and <C13>-<C17>),

·<C1> halogen atom,

·<C2> C_{1-6} alkyl,

·<C6> hydroxyl,

·<C7> C_{1-6} alkoxy,

·<C13> nitro,

·<C14> amino,

•<C15> cyano,

•<C16> carboxyl and

•<C17> $-X^1-R^{11}$ (R^{11} and X^1 are as defined above);

$R^{2'}$ is

[F] hydrogen atom,

[G] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from <G1>-<G4>, <G10>-<G13> and <G16>-<G18>),

•<G1> halogen atom,

•<G2> C_{3-12} cycloalkyl,

•<G3> hydroxyl,

•<G4> C_{1-6} alkoxy,

•<G10> nitro,

•<G11> amino,

•<G12> cyano,

•<G13> amido,

•<G16> $-PO(OH)_2$,

•<G17> $-PO(O-C_{1-6}$ alkyl$)_2$ and

•<G18> $-PO(O$-aryl$)_2$; or

[H] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <H1>, <H2>, <H6>, <H7>, <H13>-<H16> and <H19>-<H21>),

•<H1> halogen atom,

•<H2> C_{1-6} alkyl,

•<H6> hydroxyl,

•<H7> C_{1-6} alkoxy,

•<H13> nitro,

•<H14> amino,

•<H15> cyano,

•<H16> amido,

•<H19> $-PO(OH)_2$,

•<H20> $-PO(O-C_{1-6}$ alkyl$)_2$ and

•<H21> $-PO(O$-aryl$)_2$;

$R^{3'}$ is

[J] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by

1 to 3 substituents selected from the following <J1>, <J2>, <J6>, <J7>, <J13>-<J16> and <J19>-<J21>),

·<J1> halogen atom,

·<J2> C_{1-6} alkyl,

·<J6> hydroxyl,

·<J7> C_{1-6} alkoxy,

·<J13> nitro,

·<J14> amino and

·<J15> cyano

·<J16> amido,

·<J19> $-PO(OH)_2$,

·<J20> $-PO(O-C_{1-6}$ alkyl$)_2$ and

·<J21> $-PO(O$-aryl$)_2$;

$R^{4'}$ is

[K] hydrogen atom,

[L] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <L1>-<L4> and <L10>-<L12>),

·<L1> halogen atom,

·<L2> C_{3-12} cycloalkyl,

·<L3> hydroxyl,

·<L4> C_{1-6} alkoxy,

·<L10> nitro,

·<L11> amino and

·<L12> cyano;

[M] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <M1>, <M2>, <M6>, <M7>, <M13>-<M16> and <M18>),

·<M1> halogen atom,

·<M2> C_{1-6} alkyl,

·<M6> hydroxyl,

·<M7> C_{1-6} alkoxy,

·<M13> azido,

·<M14> nitro,

·<M15> amino,

·<M16> cyano and

·<M18> $-Y^{42}-R^{41'}$ ($R^{41'}$ is as defined in claim 2, Y^{42} is as defined in claim 1);

[P] 3 to 7-membered saturated heterocycle (said saturated heterocycle is optionally substituted by 1 to 3 substituents selected from the following <N1>, <N2>, <N7>, <N8>, <N14>-<N16> and <N18>),

·<N1> halogen atom,

·<N2> C_{1-6} alkyl,

·<N7> hydroxyl,

·<N8> C_{1-6} alkoxy,

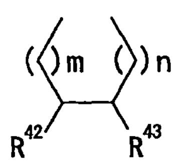
·<N14> nitro,

·<N15> amino,

·<N16> cyano and

·<N18> carboxyl; or

[S]



(R^{42} and R^{43} are each as defined in claim 1 and m and n are each independently an integer of 0 to 3) formed by $R^{4'}$ and $R^{5'}$ in combination; and

$R^{5'}$ is

[T] hydrogen atom,

[U] C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from the following <U1>-<U4> and <U10>-<U12>),

·<U1> halogen atom,

·<U2> C_{3-12} cycloalkyl,

·<U3> hydroxyl,

·<U4> C_{1-6} alkoxy,

·<U10> nitro,

·<U11> amino and

·<U12> cyano; or

[V] C_{3-12} cycloalkyl (said cycloalkyl is optionally substituted by 1 to 3 substituents selected from the following <V1>, <V2>, <V6>, <V7> and <V13>-<V15>),

·<V1> halogen atom,

·<V2> C_{1-6} alkyl,

·<V6> hydroxyl,

·<V7> C_{1-6} alkoxy,

·<V13> nitro,

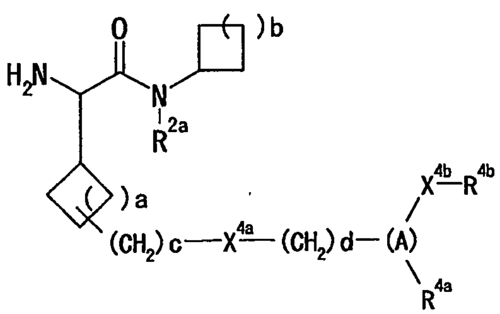
·<V14> amino and

·<V15> cyano

provided that, when R^1 and $R^{2'}$ are hydrogen atoms and $R^{3'}$ is cyclopropyl, then the combination of one of $R^{4'}$ and $R^{5'}$ being isopropyl or tert-butyl, and the other being hydrogen atom does not occur, and when R^1 and $R^{2'}$ are hydrogen atoms and $R^{3'}$ is cyclobutyl, then the combination of one of $R^{4'}$ and $R^{5'}$ being tert-butyl, and the other being hydrogen atom does not occur,

or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

5. A compound represented by the formula [III]



[III]

wherein R^{2a} is

[F] hydrogen atom or

[G] C_{1-6} alkyl,

R^{4a} is selected from the following [Mabb0], [Mabb1] and [Mabb18],

[Mabb0] hydrogen atom,

[Mabb1] halogen atom and

[Mabb18] $-X^{4c}-R^{4c}$ (R^{4c} is selected from the following (Mabba1)-(Mabba4), X^{4c} is selected from the following (Mabbb1)-(Mabbb9)),

•(Mabba1) hydrogen atom,

•(Mabba2) C_{1-6} alkyl,

•(Mabba3) aryl and

•(Mabba4) aralkyl (said alkyl, aryl and aralkyl are optionally substituted by 1 to 3 substituents selected from the following <Mabbaa1>-<Mabbaa4>),

••<Mabbaa1> halogen atom,

••<Mabbaa2> carboxyl,

••<Mabbaa3> (C_{1-6} alkoxy)carbonyl and

••<Mabbaa4> C_{1-6} alkylsulfonyl;

•(Mabbb1) single bond,

•(Mabbb2) -CO-,

•(Mabbb3) $-CO_2-$,

•(Mabbb4) -OCO-,

•(Mabbb5) $-CONR^{41c}-$,

•(Mabbb6) $-NR^{41c}CO-$,

•(Mabbb7) $-SO_2-$,

•(Mabbb8) $-SO_2NR^{41c}-$ and

•(Mabbb9) $-NR^{41c}SO_2-$ (R^{41c} is hydrogen atom or C_{1-6} alkyl);

X^{4a} is selected from the following [Lba1]-[Lba3], [Lba8], [Lba11]-[Lba13], [Lba16]-[Lba19] and [Lba21],

[Lba1] -O-,

[Lba2] -S-,

[Lba3] -CO-,

[Lba8] $-SO_2-$,

[Lba11] $-NR^{41a}-$,

[Lba12] $-CONR^{41a}-$,

[Lba13] $-NR^{41a}CO-$,

[Lba16] $-SO_2NR^{41a}-$,

[Lba17] $-NR^{41a}SO_2-$,

[Lba18] $-OCONR^{41a}-$,

[Lba19] $-NR^{41a}CO_2-$ and

[Lba21] $-NR^{41a}CONR^{41d}-$

(R^{41a} and R^{41d} are the same or different and each is hydrogen atom or C_{1-6} alkyl);

R^{4b} is selected from the following [La1], [La2], [La5] and [La6],

[La1] hydrogen atom,

[La2] C_{1-6} alkyl,

[La5] aryl and

[La6] aralkyl

(said alkyl, aryl and aralkyl are optionally substituted by 1 to 3 substituents selected from the following <Lab1>, <Lab2>, <Lab7>, <Lab8>, <Lab12>-<Lab17>, <Lab31> and <Lab32>);

·<Lab1> halogen atom,

·<Lab2> C_{1-6} alkyl (said alkyl is optionally substituted by 1 to 3 substituents selected from C_{1-6} alkoxy, $-SO_2-C_{1-6}$ alkyl, $-SO_2$-aryl, $-NHSO_2-C_{1-6}$ alkyl and $-NHSO_2$-halo-C_{1-6} alkyl),

·<Lab7> hydroxyl,

·<Lab8> C_{1-6} alkoxy,

·<Lab12> nitro,

·<Lab13> amino,

·<Lab14> cyano,

·<Lab15> carboxyl,

·<Lab16> (C_{1-6} alkoxy)carbonyl,

·<Lab17> C_{1-6} alkylsulfonyl,

·<Lab31> $-SO_2NR^{41f}R^{41g}$ and

·<Lab32> $-NR^{41f}SO_2R^{41h}$

(R^{41f}, R^{41g} are the same or different and each is hydrogen atom or C_{1-6} alkyl and R^{41h} is C_{1-6} alkyl);

X^{4b} is selected from the following [Maa1]-[Maa6], [Maa9], [Maa12]-[Maa16] and [Maa19]-[Maa21],

[Maa1] single bond,

[Maa2] -O-,

[Maa3] -S-,

[Maa4] -CO-,

[Maa5] $-CO_2-$,

[Maa6] -OCO-,

[Maa9] $-SO_2-$,

[Maa12] $-NR^{41b}-$,

[Maa13] $-CONR^{41b}-$,

[Maa14] $-NR^{41b}CO-$,

[Maa15] $-NR^{41b}CO_2-$,

[Maa16] $-OCONR^{41b}-$,

[Maa19] $-SO_2NR^{41b}-$,

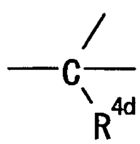
[Maa20] $-NR^{41b}SO_2-$ and

[Maa21] $-NR^{41b}CONR^{41e}-$

(R^{41b} and R^{41e} are the same or different and each is hydrogen atom or C_{1-6} alkyl, or show $-(CH_2)_2-$, $-(CH_2)_3-$, $-(CH_2)_4-$ or $-(CH_2)_5-$ together with R^{4b});

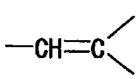
(A) is

[Mab1]



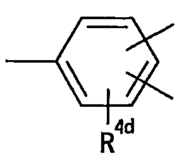
,

[Mab2]



or

[Mab5]



(R^{4d} is hydrogen atom or C_{1-6} alkyl),

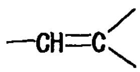
a is an integer of 1 to 4, b is an integer of 0 to 4, c is an integer of 0 to 2 and d is an integer of 0 to 4,

or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

6. The compound of claim 5, wherein (A) is

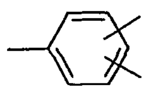
[Mab1] CH,

[Mab2]



or

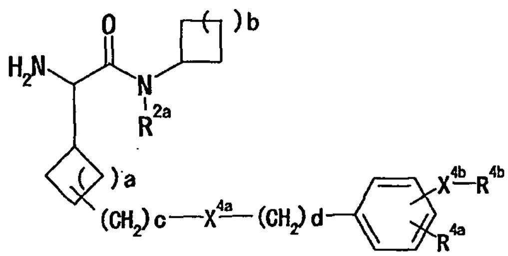
[Mab5]



,

or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

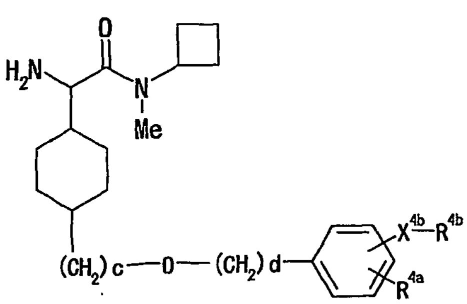
7. A compound represented by the formula [IV]



[IV]

wherein each symbol is as defined in claim 5, or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

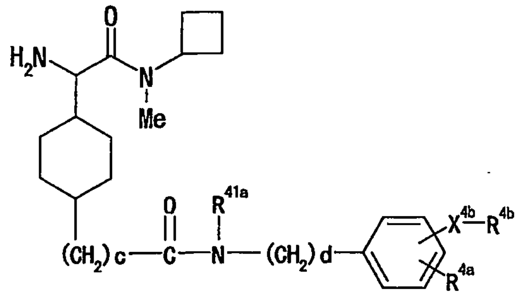
8. A compound represented by the formula [V]



[V]

wherein each symbol is as defined in claim 5, or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

9. A compound represented by the formula [VI]



[VI]

wherein each symbol is as defined in claim 5, or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

10. A compound selected from

2-{trans-4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxymethyl}benzoic acid,

2-{trans-4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxymethyl}-5-methylbenzoic acid,

3-{trans-4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxymethyl}-5-dimethylaminobenzoic acid,

4-{trans-4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxy}-3-fluorobenzoic acid,

2-{trans-4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxymethyl}-4-methoxybenzoic acid,

2-{trans-4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxymethyl}-5-fluorobenzoic acid,

3-{trans-4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxymethyl}benzoic acid,

3-{trans-4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxy}-2-methylbenzoic acid,

3-{trans-4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxy}-5-methylbenzoic acid,
3-{trans-4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxy}-5-dimethylaminobenzoic acid,
4-{trans-4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexylmethoxy}-2-methylbenzoic acid and
trans 4-[(S)-amino-(N-cyclobutyl-N-methylcarbamoyl)methyl]cyclohexanecarboxylic acid (2-methanesulfonyl)phenylamide,
or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

11. 2-{trans-4-[(S)-Amino-(N-cyclobutyl-N-methyl-carbamoyl)methyl]cyclohexylmethoxymethyl}benzoic acid or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

12. 2-{trans-4-[(S)-Amino-(N-cyclobutyl-N-methyl-carbamoyl)methyl]cyclohexylmethoxymethyl}-5-methylbenzoic acid or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

13. 3-{trans-4-[(S)-Amino-(N-cyclobutyl-N-methyl-carbamoyl)methyl]cyclohexylmethoxymethyl}-5-dimethylaminobenzoic acid or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

14. 4-{trans-4-[(S)-Amino-(N-cyclobutyl-N-methyl-carbamoyl)methyl]cyclohexylmethoxy}-3-fluorobenzoic acid or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

15. trans 4-[(S)-Amino-(N-cyclobutyl-N-

methylcarbamoyl)methyl]cyclohexanecarboxylic acid (2-methanesulfonyl)phenylamide or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

16. A pharmaceutical composition comprising the compound of any of claims 2 to 15, or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof, and a pharmaceutically acceptable carrier or excipient.

17. A drug for the treatment of diabetes, which comprises the compound of any of claims 2 to 15, or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

18. A DPP-IV inhibitor, which comprises a compound of any of claims 2 to 15, or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

19. The pharmaceutical composition of claim 16, which is used in combination with a different therapeutic drug for diabetes, a therapeutic drug for diabetic complication, a therapeutic drug for hyperlipidemia or an anti-obesity drug.

20. The pharmaceutical compossition of claim 19, wherein the different therapeutic drug for diabetes, the therapeutic drug for diabetic complication, the therapeutic drug for hyperlipidemia or the anti-obesity drug is selected from insulin preparations (injection), low-molecular insulin preparations (oral agent), sulfonylurea receptor agonists (SU drugs), short acting insulin secretagogues, α-glucosidase inhibitors, insulin sensitizers, PPARα receptor agonists, PPARγ receptor agonists/antagonists, PPARδ receptor agonists, tGLP-1 receptor agonists, glucagon receptor antagonists, glucocorticoid receptor antagonists, biguanides, SGLUT inhibitors, fructose-1,6-bisphosphatases (FBPase) inhibitors, glycogen synthase kinase 3 (GSK-3) inhibitors,

phosphoenolpyruvate carboxykinase (PEPCK) inhibitors, protein tyrosine phosphatase 1B (PTPase 1B) inhibitors, SH2 domain-containing inositol phosphatase (SHIP2) inhibitors, AMP-activated protein kinase (AMPK) activators, glycogen phosphorylase (GP) inhibitors, glucokinase activators, 11β-HSD-1 inhibitors, GPR40 receptor agonists, pyruvate dehydrogenase kinase (PDHK) inhibitors, microsomal triglyceride transfer protein (MTP) inhibitors, diacylglycerol acyltransferase (DGAT) inhibitors, cholesteryl ester transfer protein (CETP) inhibitors, HMG-CoA reductase inhibitors, β3 adrenaline receptor agonists, apolipoprotein-A1 (Apo-A1) inducers, lipoprotein lipase (LPL) activators, glucose-dependent insulinotropic polypeptide (GIP) receptor antagonists, leptin receptor agonists, bombesin receptor subtype 3 (BRS-3) agonists, perilipin inhibitors, acetyl-CoA carboxylase 1 (ACC1) inhibitors, acetyl-CoA carboxylase 2 (ACC2) inhibitors, melanocortin (MC) receptor agonists, neuropeptide Y5 (NPY5) receptor antagonists, adiponectin receptor agonists, protein kinase β (PKCβ) inhibitors, endothelial lipase inhibitors, angiotensin II receptor antagonists, aldose reductase inhibitors, angiotensin conversion enzyme (ACE) inhibitors, advanced glycation end products (AGE) inhibitors, glutamine/fructose-6-phosphate aminotransferase (GFAT) inhibitors and uncoupling protein (UCP) inducers/activators.

21. A method for treating diabetes, which comprises administering an effective amount of the compound of any of claims 2 to 15 or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof, to a mammal.

22. A method for inhibiting DPP-IV, comprising using the compound of claim 2 to 15, or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof.

23. The method of claim 21, which is used in combination with a

different therapeutic drug for diabetes, a therapeutic drug for diabetic complication, a therapeutic drug for hyperlipidemia or an anti-obesity drug.

24. The method of claim 23, wherein the different therapeutic drug for diabetes, the therapeutic drug for diabetic complication, the therapeutic drug for hyperlipidemia or the anti-obesity drug is selected from insulin preparations (injection), low-molecular insulin preparations (oral agent), sulfonylurea receptor agonists (SU drugs), short acting insulin secretagogues, α-glucosidase inhibitors, insulin sensitizers, PPARα receptor agonists, PPARγ receptor agonists/antagonists, PPARδ receptor agonists, tGLP-1 receptor agonists, glucagon receptor antagonists, glucocorticoid receptor antagonists, biguanides, SGLUT inhibitors, fructose-1,6-bisphosphatases (FBPase) inhibitors, glycogen synthase kinase 3 (GSK-3) inhibitors, phosphoenolpyruvate carboxykinase (PEPCK) inhibitors, protein tyrosine phosphatase 1B (PTPase 1B) inhibitors, SH2 domain-containing inositol phosphatase (SHIP2) inhibitors, AMP-activated protein kinase (AMPK) activators, glycogen phosphorylase (GP) inhibitors, glucokinase activators, 11β-HSD-1 inhibitors, GPR40 receptor agonists, pyruvate dehydrogenase kinase (PDHK) inhibitors, microsomal triglyceride transfer protein (MTP) inhibitors, diacylglycerol acyltransferase (DGAT) inhibitors, cholesteryl ester transfer protein (CETP) inhibitors, HMG-CoA reductase inhibitors, β3 adrenaline receptor agonists, apolipoprotein-A1 (Apo-A1) inducers, lipoprotein lipase (LPL) activators, glucose-dependent insulinotropic polypeptide (GIP) receptor antagonists, leptin receptor agonists, bombesin receptor subtype 3 (BRS-3) agonists, perilipin inhibitors, acetyl-CoA carboxylase 1 (ACC1) inhibitors, acetyl-CoA carboxylase 2 (ACC2) inhibitors, melanocortin (MC) receptor agonists, neuropeptide Y5 (NPY5) receptor antagonists, adiponectin receptor agonists, protein kinase β (PKCβ) inhibitors, endothelial lipase inhibitors, angiotensin II receptor antagonists, aldose reductase inhibitors,

angiotensin conversion enzyme (ACE) inhibitors, advanced glycation end products (AGE) inhibitors, glutamine/fructose-6-phosphate aminotransferase (GFAT) inhibitors and uncoupling protein (UCP) inducers/activators.

25. Use of the compound of any of claims 2 to 15 or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof for the manufacture of a drug for the treatment of diabetes.

26. Use of the compound of claim 2 to 15 or a stereoisomer thereof, a pharmaceutically acceptable salt thereof or a solvate thereof for the manufacture of a medicament for inhibiting DPP-IV.

27. Use of claim 25, which is used in combination with a different therapeutic drug for diabetes, a therapeutic drug for diabetic complication, a therapeutic drug for hyperlipidemia or an anti-obesity drug.

28. Use of claim 27, wherein the different therapeutic drug for diabetes, the therapeutic drug for diabetic complication, the therapeutic drug for hyperlipidemia or the anti-obesity drug is selected from insulin preparations (injection), low-molecular insulin preparations (oral agent), sulfonylurea receptor agonists (SU drugs), short acting insulin secretagogues, α-glucosidase inhibitors, insulin sensitizers, PPARα receptor agonists, PPARγ receptor agonists/antagonists, PPARδ receptor agonists, tGLP-1 receptor agonists, glucagon receptor antagonists, glucocorticoid receptor antagonists, biguanides, SGLUT inhibitors, fructose-1,6-bisphosphatases (FBPase) inhibitors, glycogen synthase kinase 3 (GSK-3) inhibitors, phosphoenolpyruvate carboxykinase (PEPCK) inhibitors, protein tyrosine phosphatase 1B (PTPase 1B) inhibitors, SH2 domain-containing inositol phosphatase (SHIP2) inhibitors, AMP-activated protein kinase (AMPK) activators, glycogen

phosphorylase (GP) inhibitors, glucokinase activators, 11β-HSD-1 inhibitors, GPR40 receptor agonists, pyruvate dehydrogenase kinase (PDHK) inhibitors, microsomal triglyceride transfer protein (MTP) inhibitors, diacylglycerol acyltransferase (DGAT) inhibitors, cholesteryl ester transfer protein (CETP) inhibitors, HMG-CoA reductase inhibitors, β3 adrenaline receptor agonists, apolipoprotein-A1 (Apo-A1) inducers, lipoprotein lipase (LPL) activators, glucose-dependent insulinotropic polypeptide (GIP) receptor antagonists, leptin receptor agonists, bombesin receptor subtype 3 (BRS-3) agonists, perilipin inhibitors, acetyl-CoA carboxylase 1 (ACC1) inhibitors, acetyl-CoA carboxylase 2 (ACC2) inhibitors, melanocortin (MC) receptor agonists, neuropeptide Y5 (NPY5) receptor antagonists, adiponectin receptor agonists, protein kinase β (PKC) inhibitors, endothelial lipase inhibitors, angiotensin II receptor antagonists, aldose reductase inhibitors, angiotensin conversion enzyme (ACE) inhibitors, advanced glycation end products (AGE) inhibitors, glutamine/fructose-6-phosphate aminotransferase (GFAT) inhibitors and uncoupling protein (UCP) inducers/activators.

29. A commercial package comprising the pharmaceutical composition of any of claims 16, 19 and 20 and a written matter associated therewith, the written matter stating that the pharmaceutical composition may or should be used for treating diabetes.